UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY
CIVIL ACTION NO 16-MD-2738(FLW)(LHG)

IN RE JOHNSON & JOHNSON POWDER PRODUCTS MARKETING, SALES PRACTICES.	:	DAUBERT HEARING JULY 30, 2019 VOLUME 7

CLARKSON S. FISHER UNITED STATES COURTHOUSE
402 EAST STATE STREET, TRENTON, NJ 08608

B E F O R E: THE HONORABLE FREDA L. WOLFSON, USDJ

A P P E A R A N C E S:

BEASLEY ALLEN, ESQUIRES
BY: P. LEIGH O'DELL, ESQUIRE (ALABAMA)
MARGARET M. THOMPSON, ESQUIRE (ALABAMA)
-and-
ASHCRAFT & GEREL, ESQUIRES
BY: MICHELLE A. PARFITT, ESQUIRE (VIRGINIA)
On behalf of the Plaintiffs Steering Committee

DRINKER, BIDDLE & REATH, ESQUIRES
BY: SUSAN M. SHARKO, ESQUIRE (NEW JERSEY)
JULIE L. TERSIGNI, ESQUIRE (NEW JERSEY)
-and-
SKADDEN, ARPS, SLATE, MEAGHER & FLOM, ESQUIRES
BY: JOHN H. BEISNER, ESQUIRE (WASHINGTON, D.C.)
-and-
PROSKAUER ROSE, ESQUIRES
BY: BART H. WILLIAMS, ESQUIRE (CALIFORNIA)
LEE M. POPKIN, ESQUIRE (NEW YORK)
-and-
WEIL GOTSHAL & MANGES, ESQUIRES
BY: ALLISON M. BROWN, ESQUIRE
On behalf of Defendant Johnson & Johnson

(Continued.)

* * * * *

A P P E A R A N C E S C O N T I N U E D

SEYFARRTH & SHAW, ESQUIRES
BY: THOMAS L. LOCKE, ESQUIRE (WASHINGTON D.C.)
On Behalf of Defendant Personal Care Products Council

M O R N I N G S E S S I O N

(In open court.)

THE DEPUTY CLERK: All rise.

THE COURT: Thank you. Good morning.

Everyone may be seated.

MS. O'DELL: Good morning, your Honor.

Your Honor, may it please the Court, we would like to call to the stand Dr. Daniel Clarke-Pearson.

DANIEL CLARKE-PEARSON, called as a witness on behalf of the Plaintiffs, having been first duly sworn, testified as follows:

DIRECT EXAMINATION

BY MS. O'DELL:

Q. Good morning, Dr. Clarke-Pearson.

A. Good morning.

Q. Would you share with the Court your field of expertise, your professional background, and some of your professional activities?

A. My field of expertise is gynecologic oncology.

I went to Harvard College and received a Bachelor's degree in biology; went to medical school at Case Western Reserve University in Cleveland, Ohio,

and then undertook my residency training in obstetrics and gynecology; and then a fellowship for three years in gynecologic oncology at Duke University Medical Center in Durham, North Carolina

Following completion of the fellowship, I joined the Duke faculty as an assistant professor; and aside from two years as director of gynecologic oncology and gynecology at the University of Illinois, I returned to Duke and then was on the faculty for another 18 years, being promoted to Professor and then the Distinguished Professor with an endowed chair. During that time I was the director of a fellowship in gynecologic oncology training fellows to become gynecologic oncologists as well.

Q. Doctor, have you devoted your career to academic medicine?

A. Yes. I have never been in private practice throughout my career.

Q. Why did you choose to do that?

A. I think for the three main reasons that we're in academic medicine, of course, to provide excellent clinical care to our patients; to teach the next generation of students, residents, fellows, and junior faculty to become excellent providers of women's healthcare; and then promote the knowledge base in our

field by conducting research. So that has attracted me to be able to do all those things. It has been very enjoyable, and I feel like I have been productive and hopefully moved the field forward.

Q. You have been asked here today to talk about the issue of talcum powder and ovarian cancer. As part of your duties as an academic physician, do you regularly teach fellows? Is that part of your normal occupational activities?

A. That's what I like to do and that's my obligation as well to teach fellows, yes.

Q. Are fellows required to master curriculum in order to become Board Certified?

A. Yes, the American Board of Obstetrics and Gynecology certifies fellows to become Board Certified. But there is a curriculum and expectations before they can take their boards to meet certain criteria and to have a certain level of knowledge above and beyond what a general obstetrician and gynecologist would have.

So the board publishes annually a bulletin that sets out the criteria or the knowledge elements that need to be part of the fellowship training program. As fellowship director for 18 years, that was my obligation, to make sure that training was

provided to those fellows.

Q. Does that training include information that talcum powder is a risk factor for ovarian cancer?

A. Yes, it does. It talks about all risk factors associated with gynecologic cancers, including talcum powder.

Q. In addition to your involvement as an academic physician, have you also devoted a lot of time and energy to professional organizations in the field of obstetrics and gynecology in general and also to gynecologic oncology?

A. Certainly. I feel a professional obligation to get outside of my ivory tower and participate in national organizations. So my primary national organization for gynecologic oncology is the Society of Gynecologic Oncology, of which I have been a member since I was Board Certified. In 2010 through '11, I was the president of the Society of Gynecologic Oncology, leading that group.

I have also been very involved with the American College of Obstetrics and Gynecology, a number of committees. I won't list them all. Probably most important in my mind is Chairing the Gynecologic Management Committee, which is a committee that writes committee opinions guiding clinical

practice for obstetricians and gynecologists and the breadth of gynecology, not just GYN oncology.

Currently I'm a member of the Society of Gynecologic Oncology's Ethics Committee.

And up until last month, I was the President of the Council of Universal Chairs in Obstetrics and Gynecology. I'm now the past president?

Q. Have you also published in the area of gynecologic cancers and also ovarian cancer?

A. Yes. I've published a little over 250 peer-reviewed publications as part of my academic interest and commitment. Most of those papers are in the field of gynecologic oncology, and some have dealt with ovarian cancer, in particular, clinical trials describing advances in the treatment of ovarian cancer.

Q. We've heard a lot about ovarian cancer, epithelial ovarian cancer. I don't think at this point in the hearing we've had someone really describe ovarian cancer. Would you take a few minutes and describe ovarian cancer, the incidence, how it occurs, the clinical course, the symptoms involved, and just give us a general overview?

A. Sure. I think there is an illustration. I think before we get into the illustration, I would

frame this by saying that ovarian cancer in the big world of cancer is a relatively rare cancer. Fortunately, I have been focused on a limited number of cancers in my career. Ovarian cancer probably occupies about 50 percent of the patients I take care of. One can argue, why is that because endometrial cancer is a much more common uterine cancer. But in 2005 I chose not to develop a skillset doing robotic surgery, and so I'm not doing surgery for endometrial cancer.

THE COURT: Let me interrupt you a second. I know you said you are not in private practice and you're associated with the medical school, but you do see patients?

THE WITNESS: Yes.

THE COURT: That was not clear from your testimony. I thought you were essentially teaching. I didn't actually know you actually saw patients.

THE WITNESS: Right.

THE COURT: Thank you for clarifying that.

BY MS. O'DELL:

Q. How much of your time over the course of your career would be involved in treating patients and teaching other physicians to treat patients?

A. While I was at Duke as fellowship director and

director of the division I was clinically active 80 percent of my waking hours, I suppose. After going to the University of North Carolina in 2005 to become Chair of the department, I cut my clinical practice about 50 percent. So I still see patients and operate 2 1/2 days a week. I hope that clarifies.

THE COURT: Thank you. I'm sorry to interrupt.

Q. You may continue.

A. With regard to ovarian cancer which occupies about half of my clinical time now, ovarian cancer, I started to say it's rare. It accounts for about 22,000 women a year developing ovarian cancer. Unfortunately, it's a disease there is no way to screen for it that we have been able to find yet, and the symptoms are vague.

So the diagnosis is not made until most patients have the disease spread well beyond the ovaries, as this illustration shows cancer growing on the surface of the ovaries. 75 percent of the time patients that we take care of are not just my patients but nationally the cancer spreads throughout the entire abdominal cavity, much like dandelion seeds in the wind will float around and land on surfaces, attach and start growing. But those symptoms are very

vague. Many patients have some vague GI symptoms, bloating, abdominal pressure, decreased appetite. Nothing that's very specific. That's why it makes it difficult to diagnose this cancer very early. So 75 percent of the time it's spread well beyond the ovary, sometimes in the Stage IV, into the liver and into the lung, and pleural space with fluid.

The treatment for ovarian cancer by and large is surgery initially to remove as much of the cancer as we can, what we call debulking, taking out the bulk of the cancer. That surgery can sometimes be very extensive, removing colon, small bowel, spleen, liver resections, lymph nodes.

THE COURT: Can you back up from the mike a little bit. Close enough that we hear you but not too close.

Q. Go ahead.

A. It's extensive surgery. And then as quickly as we can get the patient over surgery, initiate chemotherapy. The usual chemotherapy program stretches over about six months. Hopefully, the patient appears to be in remission at that time, although the majority of patients, even if they appear to be in remission, will recur most of the time within two years where we will restart, may do some more

surgery, but many times reinitiate chemotherapy, working our way through different chemotherapy regimens and experimental therapies.

The patients altogether have a survival at five years of somewhere between 30 and 50 percent of these patients that have advanced ovarian cancer I'm describing. So most will end up dying of their ovarian cancer.

Q. What are the histologic subtypes of ovarian cancer?

A. There are three general categories of ovarian cancer. The one we are talking about today is what's called epithelial ovarian cancer which is nicely illustrated in this drawing. It's a cancer that starts from the surface of the ovary, what we call the epithelium, a membrane, if you will. It expands and grows out through that surface, and we see this cancer here, but then it quickly sheds off of the ovary and spreads throughout the abdomen as I described. That's called epithelial ovarian cancer. That makes up the great majority of ovarian cancers.

There are some subtypes I'll talk about in a minute.

The second type of ovarian cancer is what's called the germ cell ovarian cancer, which is not what

we are talking about today. It's a cancer that arises in young women. The average age is about 19, where these patients with epithelial ovarian cancer the average age is somewhere 55 to 60. So germ cell cancers are a different ovarian cancer altogether.

The third cancer category that we talked about are called sex cord stromal tumors of the ovary, and, again, we're not really talking about that with regard to talcum powder.

Going back to epithelial cancers, there are subtypes. The most common is a serous histology, what they see under the microscope. There is also an endometrioid histology, a clear cell histology, and a mucinous.

So those are all lumped into the category of epithelial ovarian cancer.

Q. Is epithelial ovarian cancer a disease of one organ or is it multiple organs?

A. They talk about ovarian cancer, but I think in the last decade it's become clear that ovarian cancer is really a disease that can arise either from the ovary or the fallopian tube. And you can see in this illustration, the fallopian tube, which is right here, would lead into the uterus, which is over here, can develop malignant cells that will fall onto the ovary

and grow.

They are indistinguishable, one from the other, so fallopian tube cancer and epithelial ovarian cancers under the microscope look the same, and they can spread through what's called the peritoneum, the abdominal cavity. In some cases, we'll classify these as primary peritoneal cancer, but they are really the same cancer.

In most cases, in clinical trials, when we are doing research with chemotherapy regimens, we are treating these cancers with the same drugs. They look the same under the microscope, they act the same and respond the same to the chemotherapy regimen. So I believe they're all the same. We lump them together and call them epithelial ovarian cancer.

Q. Did you formulate opinions regarding the relationship between talcum powder products, Johnson's Baby Powder and Shower To Shower, and epithelial ovarian cancer?

A. I did.

Q. Would you please just describe for the Court your opinions, summarize your opinions.

A. I think there is a slide that might illustrate that, embellish what I have been saying, sort of bulleted points.

So after doing extensive research of the literature, I believe that genital application of talcum powder, such as Johnson & Johnson's Baby Powder and Shower To Shower, increases the risk of epithelial ovarian cancer in all women and can cause epithelial ovarian cancer in some women.

Looking particularly at the epidemiologic studies in their totality, there are many studies -- and it's only fair to look at them in their totality -- the data shows really consistent statistically significant increased risks of developing epithelial ovarian cancer after application of talcum powder to the perineum. Overall, the risk based on these epidemiologic studies is increased somewhere between 20 and 60 percent when compared to women who don't use talcum powder on their perineum.

The next point would be the mechanism is one of migration or ascension of the talcum powder from the perineum from the vulva through the vagina, cervix, uterus, and out the fallopian tube to rest on the ovary and peritoneum as the route of exposure. Inhalation is also a plausible mechanism for exposure.

The mechanism by which talcum powder causes ovarian cancer to occur is one of inflammation, and by that I mean chronic inflammation that results in

oxidative stress and then mutations of the ovarian cells become malignant. We know from animal and experimental studies and in humans that talcum powder elicits an inflammatory response.

Finally, Johnson's Baby Powder and Shower To Shower contain other carcinogens, such as asbestos, fibrous talc, platy talc, heavy metals, and fragrance chemicals that also contribute to the carcinogenicity of the product.

Q. Dr. Clarke-Pearson, you have also described in summary fashion up to this point your methodology. Would you take a few minutes and go through it in more detail, what process you undertook to reach your opinions in this case.

A. Certainly. I was asked to consider whether I think talcum powder might cause ovarian cancer. So I've started out doing a literature search, like I would to try to answer any other medical clinical question, and started looking at the epidemiologic literature, which is fairly extensive, and goes through several decades. Those include case-control studies, cohort studies, pooled studies, and meta-analyses. So lots of studies to review.

I also asked myself the question and reviewed the literature as to what the mechanism might be that

talcum powder can cause ovarian cancer. I think my steps in identifying that mechanism included the migration: How did the talcum powder get to the ovary, and then the inflammatory -- chronic inflammatory response that it caused. There is literature that we'll talk about that supports this mechanism.

Then the use of talcum powder as a risk factor. The epidemiologic data shows what the significant risk is. Then I applied a Bradford Hill causation analysis. It's much similar to what I do in medicine with an evidence-based medicine decision analysis to come to the conclusion what's best to treat a patient.

Q. Let's turn to your review of the epidemiologic literature. Did you consider the case-control and cohort studies?

A. Yes, I tried to say I reviewed everything I could possibly find, yes.

Q. On the screen you will see a forest plot. Please describe for the Court your analysis of this data.

A. I'm sure you have seen this before.

THE COURT: Many times.

A. A forest plot shows relative risks and

confidence intervals. The forest plot here includes all of these studies that are case-control studies, and these studies on the forest plot are actually three studies that are reported. I think the key to me is the relative risk on this forest plot aside from maybe just a couple of examples like this one are all to the right of 1, which means the relative risk is increased over baseline.

Nearly all of these case-control studies and nearly all of these cohort studies the relative risk is above 1. So it's an increased relative risk. Many of these studies also show statistically significant increased risk.

Q. Let's take a closer look at the top of the list of studies. One of the most recent case-control studies is the Schildkraut study. Did you review and rely on the Schildkraut study?

A. I reviewed all of the studies, Schildkraut being the most recent case-control I'm aware of. It was well done and thoughtful and addressed many issues that were not addressed in earlier studies.

MS. O'DELL: Could you pull up general causation opposition Exhibit 8, which is the Schildkraut study.

Q. Dr. Clarke-Pearson, what were the results of

this study?
A. This is a study of specifically African-American women from many regions throughout the United States. I believe it was 11. In their analysis, they concluded that genital powder was associated with the increased risk of epithelial ovarian cancer, the 44 percent increased risk that was statistically significant.

In addition, and this study compared to many other case-control studies, the investigators attempted and did look at issues with regard to dose-response, and found that there was association of dose-response, both in terms of frequency and duration, a number of lifetime applications that was statistically significant associated with the occurrence of ovarian cancer.

So in their conclusions of these African-American women, body powder was significantly associated with epithelial ovarian cancer risk, a 44 percent increase.
Q. Did these researchers comment on the mechanism by which talcum powder can cause ovarian cancer?
A. Yes. Again, in their conclusions, in their discussion, they felt it was consistent with localized chronic inflammation due to particulates that travel

through direct transvaginal route, so the migration or ascension of talcum powder to the ovaries and fallopian tubes, and that there is a dose-response observed as well.

Q. Is this description consistent with localized chronic inflammation in the ovary due to particulates that travel to a direct transvaginal route, does that support your opinion regarding the mechanism in this case?

A. This plus other information and literature supports the concept of chronic inflammation causing cancer and the transport or migration, yes.

Q. You said you considered all the studies. Did that include the meta-analyses that have been done on the literature in this case?

A. Yes, I reviewed all those.

Q. Let's go back to the PowerPoint. Is this a chart of the results of the meta-analyses?

A. Yes. All of these on the top are meta-analysis, and this is a pooled analysis by Terry. But the meta-analyses that you are asking about show basically a very consistent increased relative risk on this forest plot; and, in fact, all of these studies show a statistically significant increased risk of ovarian cancer. None of these confidence intervals overlap 1.

So these are all statistically significant with an increased risk.

Q. In your review, what weight did you place on meta-analysis?

A. A meta-analysis is one where the authors have looked at, basically brought together the existing literature, many case-control studies and cohort studies, and analyzed them all together, rather than one by one. And so I placed a lot more weight on that when you combine all of the data.

Some studies are stronger and some are weaker in those case-control studies. But giving weight to all those studies in these meta-analysis, I think it is important to be fair and honest rather than cherry picking really good studies or really poor studies. They take in everything in the literature and analyze them and come up with this forest plot, if you will, for each one of these.

The oldest study was in 1992 with only six studies in it. But over time, we added more and more information; and as we added more and more information to the number of studies, the statistical significance and relative risk stays very coherent, and the confidence intervals are actually tighter because we have more patients in them. There is more certainty

in all of these, but they are all statistically significant.

Q. You noted the most recent studies -- strike that.

The most recent meta-analyses have all the studies considered in them, one of those being Berge.

Doctor, why don't we take a closer look at the Berge study and have you walk us through the results of that analysis.

A. This is a study of the risk of ovarian cancer. So their conclusions, after doing a meta-analysis of all these studies, show that the relative risk of developing ovarian cancer associated with the genital use of talcum powder was 1.22 or 22 percent increased risk. The confidence interval of 1.13 to 1.3 is statistically significant.

They also looked at the relative risk in the case-control study specifically, and that risk was 26 percent, and for the cohort studies it was .02. So not statistically significant, but the relative risk is increased. But when they analyzed it based on one specific cell type, the serous type, which is the most common type of epithelial ovarian cancer, it was also increased in these cohort studies to 24 percent.

Q. Was that statistically significant?

A. Yes, it was statistically significant.
Q. Did they also consider dose-response in this particular study?
A. This is one of the issues that comes up in many of these cohort studies, and also the case-control studies don't really address dose-response. But other studies that do address dose-response, there was a trend to increased risk, the increased dose, the patient receives whether it is by frequency or duration of application.
Q. Did you also consider the Penninkilampi study?
A. I did. I was just talking about dose-response for a moment. This is, again, from the Berge study. So 12 of the studies had information that would be helpful in terms of understanding duration and dose-response, and that relative risk was 16 percent increased risk statistically significant.

And in seven of those studies we were able to analyze frequency of utilization of talcum powder in the genital tract, and, again, statistically significant with about a 5 percent increased risk for patients who use talcum powder more frequently.
Q. Did you consider the Penninkilampi study?
A. Yes. That was another one of the more recent meta-analysis that included 27, I believe, studies.

Q. Would you share with the Court your analysis of the Penninkilampi study?

A. Certainly.

Once again, I think this meta-analysis is fairly consistent with the Berge study, that the overall risk or risk is increased statistically to 31 percent; and in this study, again, they made an attempt to look at dose and found that there was an apparent breakpoint in patients that had more or less than 3600 lifetime applications of talcum powder. Those with more than 3600 had an overall risk of 42 percent that was statistically significant.

Q. Did they do a subgroup analysis of the cohort studies?

A. They did and again found an association with talcum powder use and serous ovarian cancer. So that one specific subtype, which is the most common epithelial ovarian cancer, the relative risk there was 25 percent.

Q. What percentage of epithelial ovarian cancers are the serous subtype?

A. The serous type make up about 80 percent of all the epithelial ovarian cancers. I mentioned endometrioid, clear cell and mucinous which make up, all together, about 20 percent.

Q. What were the conclusions of the authors in this study?
A. Well, they felt there was consistent association between the use of perineal talc and ovarian cancer.
Q. In addition to the results of the study, did the researchers also comment on the mechanism by which talcum powder could cause ovarian cancer?
A. The mechanism that Penninkilampi and his co-authors felt was the cause of talcum powder causing ovarian cancer was, again, this chronic inflammatory response which predisposed to development of ovarian cancer.

To be more specific, that includes cell injury by the talcum powder that results in oxidative stress, local increase in inflammatory mediators, such as cytokines and prostaglandins that lead to a mutation in that normal ovarian cell, epithelial cell to become carcinogenic where that cell becomes malignant.

THE COURT: Let me ask you a question. Both the Berge and Penninkilampi studies both came out in 2018?

THE WITNESS: Yes.

THE COURT: The numbers are slightly different. What were the different studies they looked at? Are there differences in the studies?

THE WITNESS: Slightly different studies.
THE COURT: Tell me what they were.
THE WITNESS: There were cohort studies that they chose to use one, Gertig in one case, and Gates in the other, I believe. Gertig and Gates were both from the Nurses' Health Study. It was the same study, the cohort study, but the Gertig and Gates analyzed it slightly differently in one. I forget which one. They assigned patients if they had never used talc or used it once a week or less, they lumped those patients together as if they didn't use talc, whereas the other one included separated low dose from never use. I think these two authors Berge and Penninkilampi -- again, they don't explain in the paper why they chose to choose one or the other.
THE COURT: Was that the only difference in the studies they reviewed while the case studies were the same?
THE WITNESS: Yes.
BY MS. O'DELL:
Q. Did the researchers in Penninkilampi conclude that there was a causal relationship between talc and ovarian cancer?
A. Yes. The statistical significance is there and the mechanism they are describing on this slide was

chronic inflammation.

Q. Let's transition for a moment, Dr. Clarke-Pearson, and have you walk us through your analysis to reach a causation opinion in this case. What was your methodology for that? Remind us.

A. My methodology was a Bradford Hill analysis.

Q. Walk us through your Bradford Hill analysis.

A. The Court has seen these factors in Bradford Hill before. But using the strength of association and consistency in my analysis, I felt there was overwhelming support in the epidemiologic literature that talcum powder statistically increased a woman's risk of developing epithelial ovarian cancer by about 30 percent, and every meta-analysis actually showed similar increases. So it was consistent.

In terms of specificity, the epidemiologic studies appears that this is specific for ovarian cancer, not other cancers, vaginal cancer, uterine cancer, and it satisfies the consideration of specificity.

Regarding temporality, in my opinion we have demonstrated and it's been shown that talcum powder exposure before the onset of ovarian cancer, so the timing is such and that for most malignancies there is a clear latency period sometimes decades from the

exposure of the talcum powder in this case to the development of obvious ovarian cancers. So it takes time to have that malignant transformation. That's the timeline that it takes. It doesn't happen in a day or two. So the temporality I believe is satisfied.

The biologic gradient and dose-response, again, some of these studies don't address dose-response, but the ones that do demonstrate that there is a dose-response both in terms of frequency of use and duration of use. There are several references there.

Going on to biological plausibility, I think it's clear talcum powder ascends from the perineum through the vagina, cervix, and uterus to the ovary. It is known as an agent to cause inflammation, and the inflammatory reaction by talcum powder on the tube and surface of the ovary results in genetic mutations that I mentioned before and then cancer. So I think that's the mechanism by which talcum powder causes ovarian cancer.

The coherence issue, I think the epidemiologic data, in vitro data that I know the Court's heard previously and experimental studies and in vivo research are consistent in explaining the pathogenesis

of epithelial ovarian cancer.

THE COURT: Having reviewed the in vivo research, and that's mostly what's there, the timing, since you have talked about the long latency period, and these studies talk about 24 hours, 48, 72 hours, explain that to me, if you can.

THE WITNESS: I'm not a laboratory researcher, those that are doing the in vitro research. But you are right. They are taking a snapshot of the exposure of talcum powder to cell lines, and those studies have demonstrated an inflammatory response. They haven't gone on to say, well, we have seen malignant transformation.

THE COURT: All of them stop short of that because none of them can do that.

THE WITNESS: I'm not sure of one that shows actual malignant transformation. I think that would take time in a laboratory, that latency period you are talking about and I'm talking about.

THE COURT: So the most that it can show is, it showed some changes in inflammatory response?

THE WITNESS: Yes, and mutations, and we see in one study single nucleotide polymorphisms. So these are mutations that are happening, and that's the next step toward malignant mutations.

So SNPs are mutations. And while there are some really significant mutations that are associated with ovarian cancer, like BRCA 1 and 2, a combination of a number of SNPs can add up to increase in the risk of ovarian cancer, and there are a number of studies that are showing that, not in vitro but in vivo, in human studies.

THE COURT: Let me ask you: During your Bradford Hill analysis, for instance, when you got to coherence you say satisfied. Obviously, on biological plausibility, you said "critical factor."

Now, you are looking at the in vitro and in vivo. Is that because you also think that is a less of a showing to you to convince you?

THE WITNESS: Would you repeat that again?

THE COURT: In looking at the in vitro and in vivo research, you say they are consistent; we know they don't get to the end point of showing transformation. So in your consideration of the factors, how much weight do you give to that factor?

THE WITNESS: I think the evidence in my view is the chronic inflammation is well established in both in vivo and in vitro studies, and that chronic inflammation then -- and we'll talk about it in a little bit more -- I think now, today, actually,

probably a decade ago was well-established as the causation for many cancers, not all, but many. So there is chronic inflammation that is well established in my opinion and in the in vivo and in vitro studies is that step towards truly invasive cancer.

THE COURT: You can continue.

BY MS. O'DELL:

Q. Would you continue, Doctor.

A. With regard to experimentation, clearly there is no randomized trials that would be unethical to do that. So if you want to talk about experimentation, we just talked about in vitro experiments that are showing this chronic inflammation, genetic mutations that are happening.

There are some sort of natural experiments, if you will, that are not randomized but evidence that tubal ligation reduces the risk of ovarian cancer that we believe is protecting that ovary from something ascending through the tube from the ovary, talcum powder, endometrial cells from the lining in the uterus. So some of those are experiments that show some protective benefit.

Likewise, use of birth control pills reduces the risk of ovarian cancer by suppressing ovulation. We'll talk about ovulation in a minute as a risk

factor.

And then analogy. I think the most straightforward in my mind is the medical literature with regard to minerals causing cancer, including ovarian cancer, but asbestos and lung cancer being the most obvious analogy to talcum powder and ovarian cancer.

Q. Dr. Clarke-Pearson, you just mentioned the term "risk factor." How do you as an academic physician define risk factor?

A. So risk factor is a factor that increases the risk of a malignancy -- in this case ovarian cancer -- and statistically increases the risk, and then in some patients goes on to cause that cancer. I think we also feel there should be a logical mechanism by which that risk factor is working. I think for ovarian cancer risk factors, we have established the mechanism in all risk factors for ovarian cancer.

Q. What is the mechanism you are referring to?

A. There are several mechanisms. I think the end result is mutation of the normal cell to become a malignant cell. We have been talking about chronic inflammation. A good number of ovarian cancers are caused by inflammation. There are other things besides talcum powder that cause inflammation, but

there is also the genetic mutation.

So the woman that has a BRCA 1 or 2 mutation has that mutation. She's inherited that mutation and is at a significant increased risk. So that's a risk factor not every woman with those mutations develops ovarian cancer, but they develop ovarian cancer in a much higher frequency than if they didn't have that mutation.

This is a list of risk factors I put together. There might be another two. The most significant is the BRCA 1 and 2 mutations increase a risk from -- the average woman in America today, has a risk of about 1.3 percent of developing ovarian cancer in her lifetime; women with BRCA 1 mutations have about a 30 to 40 percent increased risk. So a substantial increased risk.

Other risk factors on this table, family history of breast or ovarian cancer increases risk. So understanding that, it is important. Again, I think that's genetics -- and it may be other BRCA 3 or 4 that we haven't identified yet, are being passed in that family, and these SNPs that might increase the risk to 5 or 6 percent.

Q. Which of these risk factors are associated with inflammation?

A. I think starting with lifetime risk and on down through -- lifetime ovulation, retrograde menstruation, blood flowing from the uterus out through the fallopian tubes. Talcum powder products and others are probably better illustrated on this slide. So I can walk through the different sorts of reasons there is inflammation that then leads to oxidative stress and gene mutations and cancer, and all of these risk factors on this slide.

Retrograde menstruation means when the patient has their menstrual period, the menstruation, the menstrual fluid which has endometrial cells in it, instead of coming out through the cervix and vagina, some of it goes backwards, retrograde, out the fallopian tubes, into the pelvis, landing on pelvic surfaces and the ovary.

When it lands there, especially on the ovary, it's a foreign body and it causes chronic inflammation. And in some patients -- well, we know patients with endometriosis have an increased risk of developing clear cell cancer of the ovary, which is an epithelial ovarian cancer.

Obesity is an epidemic in the United States, and it is a systemic inflammatory response.

So associated with many cancers -- breast

cancer, colon cancer, but also statistically associated with ovarian cancer, and I think we understand or believe that's secondary to this chronic inflammatory response the body has to being obese. I'm not enough of a scientist to tell you why that happens, but it goes along with obesity.

Ovulation and frequent ovulation or incessant ovulation have been identified as a risk factor for ovarian cancer for decades, and I think the explanation is one, again, of inflammation and healing.

I've got a little video that might show the Court what actually happens in ovulation.

Q. Why don't you walk us through this.

A. So this is going to be an ovary. At the time of ovulation, in mid-cycle, a follicle has been developing from the last menstrual period up until about midway through that menstrual cycle. Usually midway the patient ovulates. So that follicle contains follicular fluid, and so it's -- you can see it.

It's like a little cyst or maybe a blister that ultimately -- and so the fallopian tube is over here. It's not very clear, but it's right beside it, and the idea here in normal reproduction is that egg

is going to come out of this follicle, bursts out through there. If all things go well, the fallopian tube captures this fertilization and the patient is pregnant with the embryo in the uterus. But we're just talking about ovulation right now.

So this ovulatory event, this event of ovulation -- go ahead and run the video some more. This follicle expands and ultimately, however, you want to say it explodes and that ovum comes flying out. This is the ovum in this follicular fluid. It's going to burst forth.

Now, the issue is what's happening here is whether it's a blister that's ruptured or a pimple that's ruptured, but this healing that has to happen. That's the follicular fluid bursting out, and the egg or ovum coming out. But this is where the problem lies.

This ovarian epithelium has to heal, and the healing process requires growth and stimulation. Growth factors come in here, cytokines come in, there is an inflammatory response, and then hopefully it heals. But in some cases this increases the risk of epithelial ovarian cancer by ovulating.

The evidence on the other side of the coin is if you stop ovulation by using birth control pills, by

pregnancy, by breast feeding, which stops ovulation in most cases, women that have any of those factors have a reduced risk of developing ovarian cancer. So stopping ovulation reduces the risk of ovarian cancer. So that's the inflammatory and repair process that results in ovarian cancer, the epithelium in some women.

Other things that cause chronic inflammation, polycystic ovarian syndrome is a condition that has many cysts on the ovary. Patients are infertile and obese usually as a chronic inflammatory response to that ovary.

Pelvic inflammatory disease, which is usually caused by gonorrhea and Chlamydia is successfully treated with antibiotics. So that patient that's successfully treated doesn't have a chronic inflammatory response. But some women will have chronic inflammatory disease and the epidemiology shows those patients with chronic pelvic inflammatory disease have a higher risk statistically of developing ovarian cancer.

And then talcum powder and asbestos exposure that we're talking about today, the evidence shows chronic inflammatory response to the ovary and peritoneum which then leads to this oxidative stress

production of cytokines and then gene mutations, and those mutations result in cancer.

Q. Very quickly. Are there protective factors? You mentioned one and that is reduced ovulation. Would pregnancy reduce ovulation, that would be a protective factor?

A. Yes, protective factors would be use of birth control pills. Use of oral contraceptives for five years in a woman's life reduces the risk by about 40 to 50 percent. We should be using birth control pills to prevent ovarian cancer. It is not labeled that way but it could be. Unfortunately, you think about it just as a birth control. But it could be used as a preventive, and I use it in some patients who are high risk.

Pregnancy, a woman doesn't ovulate during those nine months of pregnancy. Women that breast feed in general do not ovulate. So those reduce the risk. I mentioned previously tubal ligation and hysterectomy also reduce the risk of ovarian cancer.

Q. You have talcum powder and asbestos exposure on your slide as an inflammatory risk factor for ovarian cancer. Has it been reported in the literature that talcum powder is a risk factor for ovarian cancer?

A. Yes, widely reported in the recent literature,

yes.
Q. Let me ask you, Doctor, before we talk about some of those specific references, just to explain something to us about: Is it your opinion talcum powder causes an inflammatory response?
A. Yes.
Q. You showed the video of ovulation and the injury, if you will, to the epithelial surface of the ovary during the normal cycle. Can you explain to us how those work together, how the presence of talcum powder in that setting could intensify an inflammatory response?
A. Certainly.
Well, in some parts of the body, such as the lung, there is a clearance mechanism in the lung with mucous and cilia that gets particles out of the lung. In the ovary there is no clearance mechanism to get things out. So if talcum powder were present at the time of ovulation and it became embedded in that healing process, so that talc particle is now embedded in the ovarian epithelium, the body can't get rid of it. That is a chronic irritant and causes chronic inflammation, and there are studies that have shown talc within not just on the surface of the ovary, but in ovarian tissue.

Q. Let's transition now to some of the publications that recognize talcum powder as a risk factor for ovarian cancer. An article by Hunn and Rodriguez. Is Hunn and Rodriguez the next publication?
A. This is a review article on ovarian cancer etiology, what causes ovarian cancer, risk factors and the epidemiology.
Q. Do they include a table of the risk factors for ovarian cancer?
A. Quickly going to the table, they list risk factors here that I listed most on the other slide to simplify things. One of the risk factors they identify is inflammation, and of the inflammation endometriosis causing inflammation, pelvic inflammatory disease, but on this list they also include perineal talc exposure as an inflammatory risk factor for epithelial ovarian cancer.
Q. Also there is the Mallen reference. Are those four of the references that you reviewed and relied on in sort of evaluating whether talcum powder is a risk factor?
A. All these address talcum powder and identify it as a risk factor.
Q. Tell us about the Mallen article, please.
A. This is a relatively recent paper and it's a

review paper. It's basically addressing the risk factors.

Q. Do they include a table of the risk factors for ovarian cancer?

A. In this study the authors attempted to segregate these epithelial ovarian cancer cell types from -- separating serous from high grade serous, low grade serous, endometrioid and clear cell subtypes of epithelial cancer, and then they assign risk factors for each of these subtypes of epithelial ovarian cancer.

In all serous you can see I highlighted it. Genital powder use is a lifestyle risk factor. So something a woman would choose in her lifestyle to use or not. It's also associated with endometrioid and clear cell carcinomas. It's not clear that high grade serous and low grade serous are associated but all serous are associated with genital powder use.

The problem with some of this analysis is low grade serous is a very small number fraction of all serous cancers.

Q. Did you also consider the book chapter from Cancer Prevention and Screening by -- edited by Eeles, and did they list talcum powder as a lifestyle risk factor?

A. Yes. They sort of break it down into different risk factors. In the category of lifestyle there is other lifestyle issues that women and men can choose, whether it's alcohol use, obesity, cigarette smoking, but talc use is also listed as a lifestyle risk factor, and talc in the genital area has consistently been shown to increase the risk of ovarian cancer and is not recommended by these authors of this textbook.

Q. Lastly, Dr. Clarke-Pearson, did you consider the Vitonis publication that assessed risk factors for ovarian cancer?

A. I did. This is from 2011. So it's not brand new.

In this study the authors were going beyond just listing risk factors to adding weight to risk factors and trying to create a formula, if you will, using these eight risk factors to create a scoring system. They tried to evaluate a specific patient who might have not none of these risk factors or might have one or might have eight.

And so of the eight risk factors they included Jewish ethnicity, goes along with BRCA mutations, less than one year of oral contraceptive use, I won't read all of this, and then they added or included talc use as one of the eight risk factors that would fit into

this formula to come up with a score.
Q. Dr. Clarke-Pearson, why is it significant that talcum powder is being reported as a risk factor for ovarian cancer in the literature?
A. I'm sorry.
Q. Why is it significant that talcum powder is being reported as a risk factor for epithelial ovarian cancer in the literature?
A. Well, again, I think it's a lifestyle choice. It is not something a woman needs to do. There is just no medical indication to use talcum powder on the perineum. If it is recognized as a risk factor and a woman can choose not to use talcum powder and reduce her risk of ovarian cancer, then why not in my perceptive.
Q. Dr. Clarke-Pearson, you shared with us this morning that you've practiced in the field of gynecology for, I think, probably 40 years. Is that a fair assumption?
A. I think that's fair.
Q. Would it also be fair to say that you have done thousands of pelvic exams over your career?
A. Yes, I probably do 25 every Thursday.
Q. We heard a lot in this litigation about migration, and, specifically, there have been

arguments made by the defendants that it's impossible for talcum powder to migrate from the perineum to the fallopian tubes and ovaries. Is that true? What's your opinion? And please describe for us your reason for reaching your opinion.

A. We'll get to these articles in a second that show migration from the vagina to the ovary. I think that's quite clear.

It seems to me that the argument that's being put up is something from the perineum from the vulva from the outside skin can't get into the vagina. There is no lid or door -- I suppose if a young girl had an imperfect hymen, that might be the only way there is a barrier. Otherwise, the vulva and vagina are in continuity with each other and then in continuity with the cervix, uterus, fallopian tubes.

So it's just well accepted in the gynecology community, obstetrics and gynecology community that the conduit or the connection between the outside world and the vagina and cervix and uterus are there. It's quite obvious. There is no sphincter.

We think about the rectum. There is an anal sphincter we can hold things in with. There is no sphincter in the vagina. There is a sphincter on the urethra and we can hold in urine and we can hold in

poop with our rectal sphincter, but there is no sphincter on the vagina. So it's just open, and depending upon other factors a woman that has a baby vaginally, and the vagina opens to 10 centimeters to allow a baby to come out, that is just in continuity back and forth. So I think the gynecology community believes and recognizes that this is a direct connection.

Q. I know you've reviewed the literature, some of which is on the screen.

In addition to your training and experience and your knowledge as an academic physician who has practiced for more than 40 years, what is some of the literature that supports your opinion that talcum powder can migrate?

A. We can spend a lot or little time. These are all human experiments where the first one, carbon particles, were put in the vagina, radioactive particles were put in the vagina, glove powder just on pelvic examination came off the gloves. It was not intentionally put in the vagina. It was just glove powder.

In those three papers, migration from the vagina to the fallopian tube and ovary occurred within 24 hours. Then you could say: Well, wait a minute.

This is a particle. It doesn't have any motility to it. It's just a carbon particle or radioactive microsphere. How did it get there?

So this paper on uterine peristaltic pump, it's been well demonstrated with ultrasound that the uterus actually has -- the uterus is contracting in labor to push the baby out. But the uterus during the menstrual cycle contracts and has a retrograde so it pumps upward, if you will, and that pumping mechanism increases in the early part of the menstrual cycle until the mid-cycle, right before the follicle comes out, before the egg comes out of the follicle. That gets the maximum pumping mechanism in a retrograde fashion which pumps things up and works toward getting that egg into the fallopian tube.

It also can pump sperm, and that's intense. I think biologically, the pump is pulling sperm. If we just put sperm in the cervix and believe it is going to get to the tubes in a very short period of time, the sperm is motile, but it doesn't move that fast. The experiments with this peristaltic pump shows that sperm moves much faster than what would be expected up into the fallopian tube to hopefully achieve pregnancy because of this peristaltic pump.

So there is this pump that's going backward,

and it is a demonstration of putting microspheres on the cervix at different points in the menstrual cycle. In mid-cycle, when you want to biologically optimize pregnancy, that pump is bringing sperm up into the uterus and fallopian tubes.

So whether it's the pump bringing up sperm or bringing up talcum powder or other things, it pumps or pulls that up. It's not just a passive flow, because there's been arguments I've read where: Well, there is a flow out of the uterus, menstrual period, and that sort of thing, and that's true. But this peristaltic pump in mid-cycle, when there is not a menstrual period, is actually going the other direction, pulling things up into the fallopian tubes.

Q. Has the presence of talcum powder in the ovary been evidenced by studies of pathology?

A. Yes.

Q. Let me ask another question, just about the normal activities of a woman. Does a woman's daily activities affect particles or environmental agents entering the vagina?

A. I would think so. Let's just talk about sexual intercourse for a second. If there is talcum powder on the vulva and the woman is having vaginal intercourse, I would think it's very plausible, it's

hard to believe that it wouldn't happen that the talcum powder would be introduced into the vagina, and all these studies support the ascension migration all the way up to the fallopian tube.

Using a tampon, riding a bike or a horse, I think many of those daily activities would result in making the vagina accessible to any product that's on the vulva.

Q. Dr. Clarke-Pearson, do you understand that the FDA has written that it's indisputable that talcum powder can migrate to the ovary? Have you heard that?

A. I read that in one of their letters, yes.

Q. Is that in agreement with your opinion?

A. I think that's what I have been saying. I'm in agreement with the FDA on that topic.

Q. Let's transition from migration and talk just briefly about inhalation. Did you consider inhalation as another route of exposure to the ovary?

A. Yes. I think it's possible.

THE COURT: Possible or probable?

THE WITNESS: I think it's plausible. It's less likely than the ascension through the vagina and the genital application. I think it's much stronger.

THE COURT: But you would use the word "plausible"?

THE WITNESS: Yes.

BY MS. O'DELL:

Q. Doctor, I skipped this slide regarding the pathology studies. Is there any particular study you want to comment on?

A. I think I sort of, in answering one of your questions, said, yes, that talc has been found to be embodied in the ovaries. There are two studies up there, '71 and '96, and talc has been found in pelvic lymph nodes which had to, in my mind, ascend through the vagina and into the lymphatics and out from the pelvic organs out into the lymphatics on the pelvic side wall, and then asbestos has been found in the ovaries.

Q. Doctor, I'm going to skip a few slides here.

THE COURT: Are we finished on inhalation?

MS. O'DELL: Do you have any questions about inhalation, your Honor, other than the one you asked?

THE COURT: He just said it's plausible. I want to understand why and what you think the mechanism is?

THE WITNESS: There is evidence that talcum powder that's inhaled can migrate to the ovary through either lymphatics or through the bloodstream. It's much less likely, but I think the mechanism is there.

This is an IARC statement from, I believe, 2012 that says that inhalation and dermal contact through perineal application of talcum powders are primary routes of exposure.

THE COURT: What do you think that inhalation was based on? That comment in there, what did they rely on?

THE WITNESS: I think they are relying on -- I'm not sure. I would be speculating.

THE COURT: Thank you.

BY MS. O'DELL:

Q. Doctor, you said earlier that talcum powder causes inflammation. You mentioned in vitro studies. I think you mentioned animal studies as well.

Would you just walk through some of the evidence you are aware of in humans that talcum powder causes inflammation.

A. Sure. The inflammation question is one that I think are probably two good examples. Early in my training in the early 1970s, talcum powder was on surgical gloves, and we were told, instructed to, once we had our gloves on, and the talcum powder made the gloves go on easier, to wash the outside of our gloves.

So we would go to a basin and wash the gloves

because it was found that talcum powder that lands inside the pelvis or abdomen causes inflammation, which results in scarring, adhesions, which we didn't want to cause especially in women we are operating on where we don't want to cause adhesions in their fallopian tubes and cause infertility, and could cause granulomas, which are an inflammatory response trying to wall off talcum granules. So it's pretty good evidence in my opinion it causes inflammation.

The other part that's quite obvious and used medically even today is what's called pleurodesis where talcum powder is stuck through or a needle of some sort into the pleural space between the lung and chest wall with the intention of scarring the lung to the chest wall.

This is in situations in my patients with ovarian cancer that have fluid which is called pleural effusion in their chests, the space between the lung and the chest wall. It's filled with fluid being caused by the cancer. The patient then develops respiratory distress, and it's very uncomfortable. So we put in a chest tube, drain that fluid to let the lung expand, and then put talc in and scar the two together to prevent that fluid from reaccumulating. The mechanism by which that scarring happens is

inflammation.

Q. Dr. Clarke-Pearson, is it generally-accepted that inflammation causes cancer?

A. Chronic inflammation causes cancer.

Q. And as part of your review in this case, did you consider the Balkwill article that describes that inflammatory process? This is Exhibit 98.

So Balkwill, this was a review paper?

A. Right. This was a review paper in Lancet, which is a very prominent New England Journal, and Lancet are probably the two most prominent medical publications.

In the Lancet this review article is talking about inflammation and cancer, and it's not just ovarian cancer. It's talking about the evidence that inflammation, chronic inflammation causes a variety of different cancers.

Q. Doctor, just briefly, would you walk us through what is being depicted in terms of inflammation causing cancer.

A. This is an illustration from that review article that's sort of in a cartoon diagram, describes what's happening, starting over here on the left with normal cells. They could be ovarian epithelium, that this chronic inflammation causes tissue damage and chronic

infection, if it's pelvic inflammatory disease or chronic inflammation impacts these cells.

These cells react. They try to heal. That's the normal process. Cytokines and chemokines are created, but this process of healing doesn't always occur because there is chronic inflammation, and so cells then become mutated. And we start working our way down this process.

This is sort of a gradual progression of malignancy going from left to right. So the DNA damage that occurs by this chronic inflammation, growth stimulation. The cancer cells that are now developing don't have the same apoptosis mechanism. So programmed cell death is apoptosis, which is what normal cells go through, but cancer cells don't as much, and so they continue to grow instead of go through that cycle of programmed cell death.

Angiogenesis is cell death. For that early cancer to really take hold and grow, it needs to have a blood supply, and these malignant cells and the products that they are making, growth factors, vascular endothelial growth factors, one product being made by these cells stimulates angiogenesis, growth of blood vessels into the tumor, and also these cells are producing products that are hiding those cancer cells

from the immune system, so the immune system isn't recognizing them as abnormal.

So all of this allows the promotion and development of a malignancy. But it all starts back here at this inflammatory process.

Q. Is this process you just described also true about epithelial ovarian cancer? There have been some arguments made by defense experts that inflammation does not cause epithelial ovarian cancer. Is that true?

A. I disagree with that. And we're talking about talc today predominantly, but I showed you on the slide other things that are causing chronic inflammation, whether it's chronic pelvic inflammatory disease, endometriosis, obesity.

So chronic inflammation is what I think we believe, it's not just my belief, causes ovarian cancer in many circumstances aside from those that have gene mutations.

Q. Is there a figure from the Shan and Liu publication? Did you review this publication?

A. Yes, I reviewed this as another review article. It specifically talks about ovarian cancer.

MS. O'DELL: If we go to the figure.

Q. Doctor, briefly we talked about cancer

generally; and if you could become more specific in your discussion about how inflammation causes ovarian cancer.

A. I think this is the same representation but in a diagram form of ovulation, that rupture of the ovarian capsule and epithelium and healing process that happens here. All those cytokines and chemokines and prostaglandins that are produced in that healing process are all active right here on this ovarian surface.

If we could blow this up.

This is a diagram representation. These are epithelial cells on the surface of the ovary, and below that is the stroma or fibroblast, fibrous tissue that these cytokines, chemokines, and prostaglandins, growth factors that are out here after ovulation, and then other things that are causing inflammation, like talcum powder, impact this ovarian epithelium and stimulate the premalignant growth of these epithelial cells.

Q. Doctor, let's transition just for a moment and specifically talk about the components of talcum powder. What's your understanding of the components of talcum powder?

A. Certainly.

The majority, as I understand it, is platy talc, but it also includes fibrous talc, asbestos particles, heavy metals and chemicals that make up the fragrance of talcum powders.

Q. Is asbestos, fibrous talc and heavy metals, do you understand them to be known carcinogens?

A. Known carcinogens, yes.

Q. Do they work through an inflammatory mechanism?

A. Yes.

Q. Is that generally accepted that that's the mode by which they induce carcinogenesis?

A. Yes.

Q. Does the presence of those components in talcum powder contribute to your opinion in this case?

A. Yes, it does, but I think the epidemiology just takes talcum powder as a whole product. So what's in it is hard to identify what specifically is the carcinogen. Maybe it's all there. I don't think anybody has been able to dissect that out.

Q. Did they provide evidence of a biologically plausible mechanism by which talcum powder can cause ovarian cancer?

A. Yes. A number of carcinogens can cause and do cause ovarian cancer.

Q. Finally, Doctor, is it your opinion that the

genital use of talcum powder causes epithelial ovarian cancer?

A. Yes, it's my opinion.

Q. Do you hold that opinion to a reasonable degree of medical certainty?

A. Yes, I do.

MS. O'DELL: I have nothing further, Doctor. Thank you so much.

THE COURT: We'll take our break now and then start the cross.

You can step down, Doctor.

THE DEPUTY CLERK: All rise.

(Recess.)

(Continued on the next page.)

///

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

DANIEL CLARKE-PEARSON, resumed.

CROSS-EXAMINATION

BY MS. BROWN:

Q. Good morning, Dr. Clarke-Pearson.

A. Good morning.

Q. Doctor, to your absolute credit, you have spent the last 40 years of your professional life treating women with suspected or diagnosed gynecologic cancers. Correct?

A. Yes.

Q. And that would include ovarian cancer? Correct?

A. Yes.

Q. You have published hundreds of articles in the field of gynecologic oncology?

A. About 250.

Q. You have been a leader in some of the gynecologic oncology organizations you spoke to us about, SGO and SCOG. Correct?

A. Yes.

Q. For 40 years you have researched and taught and practiced in the field of gynecologic oncology. Fair?

A. Yes.
Q. But in over 40 years of practice, Dr. Clarke-Pearson, you have never told a patient that talcum powder caused her ovarian cancer. True?
A. That's probably true. I can't recall every single patient I talked to. I rarely had the question asked of me.
MS. BROWN: Permission to read, your Honor.
THE COURT: YES.
Q. Can we looked at B-10. Dr. Clarke-Pearson, this is from your deposition on February 4th, 2019. You were asked at line 11:
"QUESTION: Have you ever told a patient that talcum powder caused her ovarian cancer?
"ANSWER: No."
A. Okay.
Q. Dr. Clarke-Pearson, in your 40 years of practice, you have never recommended increased screening or monitoring for ovarian cancer based on a patient's prior use of talcum powder products. True?
A. That's true, because I don't ask that question.
Q. In over 40 years of practice you have never recommended that a patient undergo prophylactic surgery to remove her ovaries or fallopian tubes because of her talcum powder use. Correct?

A. That's true.
Q. The patient intake form that was in use at the University of North Carolina while you chaired the Department of Gynecologic Oncology, did not ask patients about whether or not they used talcum powder? True?
A. That's true because we feel it is not fair to make a patient feel guilty raising the issue how she developed ovarian cancer once she already has it.
THE COURT: I guess the question is, though, any of your patients that come in put aside whether they have been diagnosed with ovarian cancer, if they are coming in for appointments of any kind, is there something that's used in the questionnaire, do your forms anywhere ask that of any of the gynecological patients?
THE WITNESS: Not at this time.
Q. And, in fact, Doctor, as of the date of your deposition, the University of North Carolina and the department that you chaired for 13 years never advised women that perineal use of talcum powder can cause ovarian cancer true?
A. I have a faculty of 75 faculties, so I cannot tell you what was advised by my faculty that takes care of patients that don't have ovarian cancer.

MS. BROWN: Permission to read, your Honor.

THE COURT: Yes.

Q. This is B-10, your February 4th, 2019, deposition in this matter, page 96, lines 5 through 10. You were asked, Doctor:

"QUESTION: As of today, the University of North Carolina and the department that you chaired do not advise women that perineal use of talcum causes ovarian cancer. Correct?"

There was an objection.

"ANSWER: That's correct."

A. Maybe I misunderstood the question as: Was I advising? I don't know what my faculty advised.

Q. You have never advised your patients that talcum powder use causes ovarian cancer?

A. So the answer from me and my patients who have ovarian cancer, no, I don't advise them because I think that would just add to their mental anguish and guilt, that maybe they caused something which they may have. It's not going to help me take care of that patient that has ovarian cancer.

Q. Your patients are moms and sisters and aunts, and you don't advise them that they should not be purchasing an over-the-counter product for their family that you believe causes ovarian cancer. True?

A. That's true.
Q. You have given a number of presentations over the course of your career, but you had never given any presentation anywhere on the relationship between talcum powder and ovarian cancer. Correct?
A. I believe there is a chapter I wrote in 1985 that references talcum powder as a possible risk for ovarian cancer.
MS. BROWN: Permission to read, your Honor.
THE COURT: Yes.
Q. At your February 4th, 2019, deposition, you were asked:
"QUESTION: Have you ever given any presentation on the relationship between talcum powder and ovarian cancer?
"ANSWER: No."
You have also, Dr. Clarke-Pearson, published a number of articles on ovarian cancer. Correct?
A. Yes. You have to show me which ones you want to talk about. Most are clinical trials and treatment.
Q. None of those articles discuss your theory that talcum powder causes ovarian cancer?
A. That was not the intent of any of those articles.
Q. So the answer to my question is correct, none of

your articles discuss your theory talcum powder causes ovarian cancer. True?

A. That's right, because that's not the intent of any of those articles.

Q. You would agree with me, Dr. Clarke-Pearson, and I heard you mention it this morning, that the potential association between talcum powder and ovarian cancer has been reported in the literature for decades. Correct?

A. That information has been gathering over time.

Q. And, in fact, at your deposition you told us that you yourself have been aware of the potential association since your residency back in 1975. Correct?

A. That's true.

Q. But the truth is, Dr. Clarke-Pearson, that it wasn't until the end of 2018, after you were hired by the plaintiffs' lawyers, that you formed the opinion that talcum powder causes ovarian cancer. True?

A. No. I formed my opinion before I was hired by the lawyers.

MS. BROWN: Permission to read, your Honor.

THE COURT: Yes.

Q. At your February 4th, 2019, deposition, page 104, lines 3 through 24, you were asked -- talking

about a video that we will talking about in a little bit:

"You did not tell the viewers that talcum powder was associated with a cause of ovarian cancer. Is that right?

"ANSWER: That's correct. Because at that point in time I didn't believe it was causative.

"QUESTION: It wasn't until after being retained in this case and around the time that you concluded your review in November of 2018, that you formed that opinion."

There was an objection.

"ANSWER: As I was preparing to offer an opinion I did this review and came to that opinion, yes.

"QUESTION: If we try to put a time on it, it would be toward the latter part of 2018, once you had completed your review that you told us about in connection with this litigation. Correct?

"ANSWER: Yes."

I want Dr. Clarke-Pearson --

A. Can you tell me when the video you are referencing the very time is?

Q. I'll ask you some questions about it. We're going to get to it. Right now I want to talk about

some other publications you had in your field over the years.

In 1993 you authored a publication regarding mutations of the p53 gene and ovarian cancer. Do you recall that?

A. Not really. I was a co-author and that was a long time ago. Do you have that in the exhibits?

Q. Absolutely. You were asked about this paper at your deposition a few months ago. Do you recall that?

A. I do.

Q. You can find it in your binder up there, Dr. Clarke-Pearson, at tab 501. We'll also bring it up on the screen to aid you.

Do you recall, Dr. Clarke-Pearson, talking about this article a few months ago in your deposition and --

A. I'm not listening to you while I'm trying to find this.

MS. BROWN: May I approach to help him?

THE COURT: Yes.

(Pause.)

Q. Have you got that in front of you?

A. Yes.

Q. This was an article you were a co-author on back in 1993 regarding the p53 gene in ovarian cancer.

Correct?
A. Correct.
Q. And one of the things that you note in this article is that approximately one-half of human epithelial ovarian cancers have mutations in the p53 gene. Correct?
A. That's what we found.
Q. And what you concluded in this article with your co-authors back in 1993 is that "p53 mutations in ovarian cancer arise because of spontaneous errors in DNA synthesis and repair rather than a direct interaction of carcinogens with DNA. These molecular data you and your co-authors noted here in your article, these molecular data are consistent with data from epidemiologic studies that have failed to demonstrate a convincing relationship between exposure to environmental carcinogens and the development of ovarian cancer."

That's what you wrote in 1993. Correct?
A. That's what my lead author wrote and I was a co-author, yes.
Q. Doctor, just to orient us as we walk through your field and testimony, you told us a moment ago you first became aware of the potential association of talc and ovarian cancer during your residency in 1975.

True?
A. That's right, based on Johns Hopkins data from Woodruff and Parmley.
Q. We just looked at an article from 1993 which you were a co-author on in which you concluded that most environmental carcinogens are not linked to p53 mutations. Right?
A. That's what that article said, yes.
Q. I want to take a look at another article that you wrote, Dr. Clarke-Pearson, in 2009, and you can find that in the very next tab in the binder in front of you at 502. This is an article -- if we can bring it up on the screen -- that you were in fact the sole author of. Correct?
A. This is an invited review article from the New England Journal, and I was the sole author, yes.
Q. And the New England Journal of Medicine we can agree is a prestigious medical journal. Correct?
A. I said that earlier, yes.
Q. The article here is entitled, "Screening For Ovarian Cancer." Correct?
A. Yes.
Q. One of the things you were telling us earlier today is that by the time you treat patients, they in many cases already have ovarian cancer. Correct?

A. Yes.
Q. But part of your research and the focus of your 40 years in this area has also been on how to screen women for ovarian cancer and how to prevent women from getting ovarian cancer. Correct?
A. Yes.
Q. And in this particular article you posed a hypothetical -- you were posed a hypothetical at the beginning, and the article deals with circumstances in which a physician should consider screening a woman for ovarian cancer. Correct?
A. No. It is not intended -- the article concludes that we are not able to screen for ovarian cancer. So I was not encouraging physicians to screen for ovarian cancer because there was no mechanism in 2009 or in 2019 on how we can screen for ovarian cancer.
Q. I'm not trying to quibble with you on this.
A. I'm just stating what this article is intended to say.
Q. Let's see if we can understand each other, what this article is about.
The article starts out with a description of a putative plaintiff who has come to her physician with this description. Fair enough?
A. That's the case.

Q. And you review throughout the article the state of knowledge of ovarian cancer, and you include a discussion of some risk factors for ovarian cancer. Correct?
A. Some risk factors.
Q. And your ultimate conclusion in this article is this woman should not be screened for ovarian cancer. Correct?
A. Because we don't have any screening methods to use. So why would we screen.
Q. That's unfortunately one of the terrible things about ovarian cancer is that we don't have a way to screen women for ovarian cancer. Correct?
A. That's correct.
Q. And what you note in connection with this article, Doctor, is you comment on that very thing. And if we could look at page 2, second column, top paragraph, one of the things you are talking about is that because there is no obvious precursor lesion, screening has to focus on early detection of invasive cancer. Correct?
A. Where does it say "early detection"?
Q. Very top. Because there is no obvious precursor lesion. Are you with me?
A. Yes. That wasn't highlighted.

Q. "Screening must focus on early detection of invasive cancer." Correct?
A. That's the whole idea of any screening for cancer.
Q. What you go on to state in this 2009 article in the prestigious New England Journal of Medicine is that risk factors other than age, a family history of ovarian or breast cancer, and the presence of a BRCA mutation are poorly understood, and approximately 90 percent of ovarian cancers appear to be sporadic. Correct?
A. Yes.
Q. In this 2019 article, 2009 article in the New England Journal of Medicine, you made no reference to talc as a causative agent or a risk factor for ovarian cancer. True?
A. There are a number of other risk factors that we didn't include in that study because, again, you can't screen for ovarian cancer.
Q. In your 2009 article in the New England Journal of Medicine you make no reference to talc as a causative agent in ovarian cancer. Is that correct, Doctor?
A. I didn't make the reference to that or didn't make the reference to incessant ovulation,

endometriosis, pelvic inflammatory disease, for example.

Q. In fact, what you did is you called out three risk factors, right? Age, family history, and BRCA mutation. Correct?

A. Yes.

Q. And for the others you wrote that they are poorly understood. Correct?

A. Yes.

Q. In 2011, Dr. Clarke-Pearson, you did some work with the Society of Gynecologic Oncologists as you have over the course of your career. Correct?

A. Yes.

Q. And you were part of a publication which can be found at 530 in your binder -- and if we could bring that up -- called "Pathways to Progress in Women's Cancer, a Research Agenda Proposed by the Society of Gynecologic Oncologists."

Just to orient us, Dr. Clarke-Pearson, you have held some leadership positions in that organization, including being the president. True?

A. Correct.

Q. And in this particular publication, Pathways to Progress from 2011, your name appears here on the first page as the immediate past president of this

Society. Correct?
A. Yes, as a cover letter to the membership.
Q. If we could look at the first paragraph of the cover letter to this publication, you and the then president write in the third sentence, you give a little context for what this report is in fact about, and you say:
"To make our vision a reality, SGO has in this research report entitled, Pathway to Progress In Women's Cancers, identified and outlined the areas of research by diseases upon which the women's cancer community should focus for the next decade."
Do you see that, Doctor?
A. Yes.
Q. So part of this publication, what this was to progress in women's cancer was to identify areas of research and to improve research and study in the field of gynecologic cancers. True?
A. Certainly, that's what we want to do.
Q. And on page 17 of this document, Doctor, one of the things that you write about is similar to what we have been talking about, the idea that screening for ovarian cancer is notoriously difficult. Correct?
A. Yes.
Q. And you have a section in this publication from

2019 that talks about how to prevent ovarian cancer or what preventive action could be taken. Correct?

A. Yes.

Q. And in this section entitled "Prevention in 2019," you make mention of a number of risk factors for ovarian cancer. True?

A. These are high risk factors, true.

Q. And those risk factors that you included in this 80-page Pathways to Progress document states as follows:

"Family history and inherited risk are the strongest risk factors for the development of ovarian cancer but they cannot be modified. Obesity is a known risk factor for the development of ovarian and many other cancers."

Do you see that?

A. Yes.

Q. You go on to talk about protective factors for ovarian cancer. Is that correct?

A. Yes, and I talked about them earlier today.

Q. Mr. Williams reminded me that I did not say the year of this publication, but it was from 2011. Correct?

A. Yes.

Q. So in 2011, this publication from the Society of

Gynecologic Oncology, which mentions prevention of ovarian cancer and risk factors, did not include any discussion of talc as a causative agent for ovarian cancer. Correct?

A. That's not shown there, yes.

Q. And the purpose or at least the title of this document is "Pathways to Progress in Women's Cancer." Correct?

A. It's encouraging us to continue research to find, for example, screening methods, other ways to prevent ovarian cancer, better ways to treat it. It was a comprehensive outline how we would like to progress, and it was intended for many audiences, including the National Cancer Institute that was not funding cancer research adequately in our opinion.

Q. We will talk about the NCI a little bit later. In the Pathway to Progress, a Research Agenda Proposed for the Society of Gynecological Oncology, in which your name appears in 2011, this document made no mention that talc causes ovarian cancer. Correct?

A. From what you have shown me. I can't recall this whole thing from 2011. You implied I'm the author. I'm not the author of this publication.

Q. At this time you were the immediate past president of this Society. Correct, Doctor?

A. I was immediate past president. I wasn't the author of this publication.
Q. And you authored the cover page of the document that follows. Correct?
A. Yes.
Q. And you referred to this research report as an effort to outline areas of research in which the women's cancer community should focus for the next decade. Correct?
A. We're trying to develop an agenda for a variety of audiences to encourage research, to improve the outcomes of women with ovarian cancer.
Q. And you made no mention in your cover letter or in the document itself of talc causing ovarian cancer. Correct?
A. And other risk factors, that's true.
Q. Now, in 2014, Doctor, you appeared on a Fox News interview. Do you recall that?
A. Yes. It was in Greensboro, North Carolina, a very brief morning piece for women that are doing the laundry that lasted about two minutes maybe.
Q. And I imagine you were also interested in reaching women who were not doing the laundry. This was an effort to reach all women --
A. Anyone who was available at 10 o'clock in the

morning, yes.
Q. But it was an effort to get the word out about ovarian cancer, for all women, regardless of whether they were folding the laundry at 10 o'clock?
A. Exactly. Anybody who was listening, I was happy to have them hear me.
Q. I would like to take a look at it and ask you a couple of questions about it, if we could.
(The video was played.)
Q. Now, Dr. Clarke-Pearson, we can agree, of course, on this television interview, one of the things you were endeavoring to do is to help women. Right?
A. Absolutely.
Q. You go on in that interview to encourage women, if they think they have signs of ovarian cancer, to go to their doctor and ask to be checked out. Right?
A. That's correct.
Q. And one of the things you said here is "I hope this clip encourages women to get better care and to detect ovarian cancer earlier." Right?
A. Yes.
Q. One of the things you did in connection with your effort to help women is you listed some of the risk factors for ovarian cancer. Correct?

A. I listed some of the high risk factors, yes.
Q. You did not advise the Fox viewers in 2014 that they shouldn't go to the drugstore and buy talcum powder because it causes ovarian cancer. Correct?
A. That was not mentioned along with a lot of other things.
Q. And the reason you didn't mention that, Dr. Clarke-Pearson, in 2014 is because in 2014 you didn't believe that talc causes ovarian cancer?
A. I didn't believe it, but there was certainly mounting evidence that we had to start thinking seriously about that issue.
Q. In 2014, Doctor, five years ago, you did not believe the opinions that you've come into this courtroom to give us today. You did not believe that talc causes ovarian cancer?
A. I've learned a lot in the last two years.
Q. In fact, it wasn't until you became an expert in this litigation that you came to believe that talc causes ovarian cancer. Correct?
A. I became an expert after I believed that talc caused ovarian cancer, not the other way around.
Q. Well, let's talk a little bit about how you got involved in this litigation.
You know one of the plaintiffs' lawyers.

Correct?
A. Yes.
Q. You actually went to medical school with Dr. Thompson. Correct?
A. Not true.
Q. You were at medical school at the same time. Correct?
A. I was a resident in obstetrics and gynecology when Dr. Thompson was a medical student, and I didn't know her at that time.
Q. And it was through Dr. Thompson you got involved in this litigation. Correct?
A. She asked me if I would evaluate whether I believed talcum powder caused ovarian cancer or not before I started in on my methodologic review of the literature.
Q. At the time Dr. Thompson approached you, you had been a practicing gynecologic oncologist for 40 years. Correct?
A. Thereabouts, yes.
Q. At the time Dr. Thompson approached you, you did not hold the opinion that talcum powder causes ovarian cancer?
A. I didn't hold an opinion at that time. That's true.

Q. Dr. Thompson approached you in late 2017, early 2018. Correct?
A. I don't recall exactly when.
Q. It wasn't until after you did a review for Dr. Thompson that you came to the opinion that you now hold here today. Correct?
A. I did a review for myself. I'm not going to go out and do something for Dr. Thompson because she wants me to say something for her or her firm. I have a reputation, and I feel it's a strong reputation, and I'm not going to sign on as somebody's hired gun. So I reviewed the literature in depth and came to the conclusion talcum powder causes ovarian cancer.
Q. You were compensated, of course, to review the literature. Correct?
A. After I made a conclusion as to what my position was, yes.
Q. And you submitted an invoice for your review of that literature. Correct?
A. Yes.
Q. And you were compensated by the plaintiffs' lawyers. Right?
A. As every expert witness.
THE COURT: Did you serve as an expert?
THE WITNESS: Witness, not in a product

liability, but in many malpractice cases.

THE COURT: Not in a case like this before?

THE WITNESS: No.

BY MS. BROWN:

Q. And so if we can work a little bit with timing and this board, Doctor, is it fair to say after Dr. Thompson approached you about being an expert in litigation and you reviewed the literature, you came to the opinion that talcum powder causes ovarian cancer. Correct?

A. Yes, after doing a Bradford Hill analysis.

Q. And prior to that, though, prior to that time, though, Dr. Clarke-Pearson, you were not of that opinion. Correct?

A. I was not of that opinion.

Q. I want to talk a little bit about whether or not this opinion that you've come to hold in the last couple of years after getting involved in this litigation, whether that opinion is generally-accepted in your gynecologic community.

I want to start by talking about the American College of Obstetrics and Gynecology. You would agree, Dr. Clarke-Pearson, that that is a leading organization in your field. Correct?

A. Yes, in obstetrics and gynecology.

Q. It is one of the premier medical associations for doctors like yourself who have dedicated their professional life to gynecological oncology?
A. The American College of Obstetrics and Gynecology is more for general obstetricians and gynecologists, and the Society of Gynecologic Oncology is the premier organization for gynecologic oncologists.
Q. We're going to talk about that one next. I want to start with the American College of Obstetrics and Gynecologists otherwise known in your field as ACOG. Correct?
A. Correct.
Q. You have been a member of ACOG for decades. Correct?
A. Yes.
Q. You have led numerous postgraduates and continuing education courses sponsored by ACOG. Correct?
A. Yes.
Q. You have served on a number of ACOG committees. Correct?
A. Yes.
Q. You spoke about that with counsel this morning. The gynecologic management committee is one of those.

Correct?
A. That's correct.
Q. You have also served a three-year term on the ACOG executive board. Correct?
A. Yes.
Q. And as a practicing gynecologic oncologist, one of the places you look for guidance regarding potential risk factors for ovarian cancers are professional organizations like ACOG. Correct?
A. They serve an educational role for general obstetricians and gynecologists.
Q. You know ACOG does not recognize talc as a causative agent of ovarian cancer. Right?
A. You have to show me the publication.
Q. I'll be happy to.

Let's take a look at, if we could -- and it's in your binder, sir. If you want a hard copy there, at 515. I think we have a slide we can probably use for this.

Now, one of the things you know, Dr. Clarke-Pearson, is that ACOG has a patient facing website, and we spoke about it in your deposition regarding risk factors for ovarian cancer. Correct?
A. Yes.
Q. And this website that ACOG, one of the leading

organizations in your field, maintains is frequently updated to stay up to date on the latest medical and scientific information. True?

A. Yes.

Q. And this page that we're looking at right now is entitled, "What are the risk factors for ovarian cancer?" Correct?

A. Yes.

Q. And we can see that this particular one was updated just a few months ago, in April of 2019. Correct?

A. Yes.

Q. And ACOG lists a number of risk factors for ovarian cancer. True?

A. Yes.

Q. Some of these we have seen in your own publications: age, family history, BRCA mutations. Correct?

A. Yes.

Q. And some of these are new for us here, never having had children. Correct?

A. I'm sorry?

Q. New for our discussion this morning. We have not yet seen a publication listed, never having had children, though, it's on ACOG's website?

A. It has been in publications over the years before this. In our discussion, this is a new topic such as Lynch Syndrome, and other things.

Q. We can certainly agree ACOG does not list talcum powder as a risk factor for ovarian cancer. Correct?

A. We can agree.

Q. And certainly ACOG does not advise its people who come to its website or look to it for scientific advice, certainly does not advise that talcum powder has been established as a cause of ovarian cancer. Correct?

A. They haven't published that, no.

Q. And one of the things that ACOG has done for people that look to ACOG for guidance is it in fact puts out a statement regarding the alleged association between talcum powder and ovarian cancer. Correct?

A. You have to again point me to that publication.

Q. Sure. In your binder, it is No. 523, and if we could look at the entire document for a second, so we can orient ourselves as to who this is from and what is going on here.

What we see here, Doctor, is that in September of 2017, the Executive Vice President and CEO of ACOG, Dr. Lawrence, released the following statement on talc use and ovarian cancer. Correct?

A. Yes.

Q. And let's take a look at what the statement of this leading gynecologic organization had to say. If we're able to blow that up, that would be great.

"Despite an observed association several decades of medical research have not demonstrated a direct causative link between the use of talcum powder and ovarian cancer. Although some case control studies suggested an association, with a small increase in risk, prospective cohort studies have not demonstrated an increased risk. It is important to note that there are limitations associated with the studies that have investigated this association, which includes several types of bias, inadequate sample sizes, and the rarity of the disease. Because of concerns regarding potential discomfort or pain, obstetrician gynecologists do not recommend use of vaginal treatments such as douche, vaginal sprays, or talcum powder, and the use of talcum powder has declined over the years. There is no medical consensus that talcum powder causes ovarian cancer."

That was the statement from the Executive Vice President and CEO of ACOG in September of 2017. Correct?

A. Yes. I'll disagree with that, but that's what

he said.
Q. And one of the things that ACOG does in addition to providing information to potential patients or women with ovarian cancer or suspected ovarian cancer is it also provides information for clinicians. Correct?
A. Yes.
Q. And one of the things that's available on ACOG's website is a PowerPoint presentation about ovarian, peritoneal and fallopian tube cancer. And I would like to ask you some questions about that. You can find it in your binder at tab 532.
Now, for this PowerPoint ACOG distributes for clinicians it actually goes beyond established risk factors and also identifies some suspected or possible risk factors. Do you see that, Doctor?
A. Yes.
Q. And this updated presentation is from January of 2017 and nowhere in the established or even suspected or possible risk factors does ACOG identify talcum powder as a risk factor for ovarian cancer. True?
A. That's true. It's not on this slide. I had nothing to do with this slide. I don't want you to imply because I was a member of some committees on ACOG at one point in time that I had anything to do

with Dr. Lawrence's statement or this PowerPoint. I'm not responsible for any of this.

Q. I definitely want to be clear on that. As of today, you disagree with ACOG on this score. Correct?

A. Yes.

Q. When Dr. Lawrence made his statement, though, back in 2017, before you were hired as an expert in this litigation, you were of the view that talcum powder had not been established as a cause of ovarian cancer. True?

A. It was not my view in 2017 because I hadn't done the research that I've done now.

Q. I would like to take a look at the most recent statement from ACOG on this score, and it comes out of your former committee, the Gynecologic Management Committee. This is a committee opinion that can be found in your binder, Doctor, at 540.

Now, one of the things that the ACOG committees, including the ones on which you served, do from time to time is they issue committee opinions. Correct?

A. Yes.

Q. In fact, your resume lists some of the many opinions of which you were a part of during your time in service on the Gynecologic Management Committee.

Correct?
A. That's right.
Q. And in 2019, ACOG's Gynecologic Management Committee in fact recommended the use of talc following gynecologic surgery in obese women. Do you see that?
A. This is recommended to help an abdominal wound heal, by closing inflammation and scarring and closure to avoid seromas forming in obese women who have thick layers of fat. It has nothing to do with vaginal talc.
Q. The Gynecologic Management Committee on which you once served has recently this year recommended the use of talc for women who had undergone gynecologic surgery. Were you aware of that?
A. Yes. We're talking about abdominal incisions to help them close and heal and not fall apart after surgery in obese patients. It has nothing to do with perineal use. They were not advising putting talc in the pelvis after pelvic surgery.
Q. That wasn't my question. I just want to know if you were aware that the committee on which you once served as recently as this year is recommending the medical use of talc?
A. Yes, I was aware of that.

Q. I want to talk about the Society of Gynecologic Oncologists or SGO. You are familiar with that organization. Correct?
A. Yes.
Q. And you have been a member of SGO for decades?
A. Yes.
Q. You in fact were the president of SGO from 2009 to 2010. Correct?
A. That's correct, '10 to '11.
Q. SGO describes its mission as promoting excellence in the care of women at risk for or affected by gynecologic cancer through advocacy, education, research and interdisciplinary collaboration. Right?
A. It sounds like our mission statement.
Q. And you would agree, of course, Dr. Clarke-Pearson, that the doctors and the scientists at SGO are working very hard to protect women's health. Correct?
A. Yes.
Q. And you know that just like ACOG, SGO makes available for a potential patient's or healthcare provider's information about the potential risk factors for ovarian cancer. Correct?
A. Yes.

Q. And you know that SGO does not identify talc as a risk factor for ovarian cancer?
A. That's my understanding, yes.
Q. And you know most certainly SGO does not identify talc as an agent that has been identified as causing ovarian cancer. Correct?
A. That's what I understand, yes.
Q. Let's take a look at the SGO website, and we can go to the slide for these.
Now, SGO, as you know, Doctor, actually has quite a robust list of potential risk factors. Correct?
A. I don't know what you mean by that.
Q. Well. We had to put it on two slides. Let's take a look at what SGO advises. They list, as we've discussed, the BRCA mutations. Correct?
A. Yes.
Q. They list Lynch Syndrome as a potential risk factor?
A. Yes.
Q. And they list family history. Correct?
A. Yes.
Q. If we can go to the second slide, their list continues to include a number of different risk factors for ovarian cancer, including age,

endometriosis, personal history of breast cancer. Correct?

A. Yes.

Q. Nowhere on this two-page list from SGO of potential risk factors of ovarian cancer does talcum powder appear. True?

A. That's true. Can you tell me when this was published?

Q. Absolutely. This list is currently -- as we downloaded it on September 12th, this is currently available on SGO's website.

A. Okay.

Q. I want to talk about the Centers for Disease Control and Prevention. You are aware that they also advise people looking to them as a resource of potential risks factors for ovarian cancer. Correct?

A. Yes.

Q. And if we could take a look at that slide.

Doctor, this is at tab 516. This is what the Centers for Disease Control and Prevention advises anyone who comes to its website, as recently as June 12th, of the risk factors of ovarian cancer, and they include some of the many that we looked at this morning. Correct?

A. Yes.

Q. Age, right? Middle age or older?
A. Yes.
Q. BRCA mutations, which we looked at, endometriosis. Correct?
A. Yes. All those things are on there, listed.
Q. You know the CDC does not advise anyone going to its website or looking to it as a source of scientific information, does not advise that talcum powder causes ovarian cancer. Correct?
A. That's correct.
Q. And, in fact, the CDC actually recommends the use of talcum powder in the genital area. Does it not?
A. I'm not aware of that.
Q. Let's take a look at the slide for us, and it's tab 541 in your book, Doctor.

Are you aware the CDC in 2015 put out some guidelines related to sexually transmitted diseases?
A. I'm not aware of that. I'm reading along with you.
Q. One of the sexually transmitted diseases the CDC deals with is genital warts. And the CDC, as recently as 2015, advised of a potential treatment for genital wart pain, and what it said is that if the pain is intense, powder the genital area with talc. Do you

see that, Doctor?
A. Yes, they were talking about a short-term treatment for pain, not some chronic use, on a daily or weekly basis.
Q. Well, the CDC doesn't say: Be careful not to use this too long because it causes ovarian cancer; does it?
A. Are they are talking about treating the pain? Once the pain goes away, one would assume the patient would stop using the treatment listed here, including baking soda.
Q. The CDC does not advise you should weigh the risks of using talcum powder for your pain because we, the CDC, believe it causes ovarian cancer. Correct?
A. That's correct.
Q. You mentioned a little earlier this morning "NCI." Do you remember that?
A. I may have said "NCI." In what context?
Q. In the context of looking for a governmental organization to sponsor ovarian cancer research, you were organizing efforts to get NCI to give more money for ovarian cancer research.
A. That was at SGO.
Q. And the NCI is a part of the National Institutes of Health. Correct?

A. Yes.
Q. And, in fact, some of your research has been funded by NCI over the years. Is that correct?
A. That's correct.
Q. And one of the things the NCI does is it produces guidance for physicians on the risk factors for cancer. Are you aware of that?
A. No.
Q. Let's take a look, if we could, in your binder, Doctor, at 517. If we could bring up the actual document which is 517 and page 1.

This is a printout from the NIH, NCI website regarding ovarian, fallopian tube and primary peritoneal cancer prevention, and this is at the health professional version. Do you see that, Doctor?
A. Yes.
Q. Did you know that NIH put out a publication like this?
A. I was not aware of it.
Q. One of the things NIH and NCI do here is they review the strength of the evidence for some potential risk factors. And if we could take a look at page 12, please, they have identified factors with inadequate evidence of an association of ovarian, fallopian tube, and primary peritoneal cancer. Do you see that there,

Doctor?

A. Yes.

Q. One of the things this document from the National Institutes of Health through the NCI that has funded some of your research does is it identifies factors that have inadequate evidence of an association with perineal area risk of ovarian cancer. Do you see that?

A. Yes.

Q. One of the factors with inadequate evidence that NIH and NCI identified here is perineal talc exposure. True?

A. Yes.

Q. And what the government cancer agency that we're looking at, what they conclude here is that "the weight of evidence does not support an association between perineal talc exposure and an increased risk of ovarian cancer."

Do you see that?

A. And the references are out of date based on today's discussion.

Q. Let's take a look at when this document was updated by the NIH, NCI, and we can find that at page 18?

See down there at the bottom the word

"updated." This was updated May 30th, 2019. Do you see that, Dr. Clarke-Pearson?

A. I see that. It doesn't mean it was really adequately updated. The meta-analysis that we talked about this morning were in 2018, and they are not included in this manuscript in terms of references.

Q. Have you seen this before?

A. No. I'm quickly looking at the reference list of 50 references.

Q. I want to make sure you have enough time to look at it.

A. You are talking to me, and I'm trying to read.

Q. I just want to direct your attention when you get there, Doctor, to the updated date. Are you with me?

A. I'm not sure where you are now. Where are you?

Q. Page 18 of 19 --

A. The date this was updated?

Q. Correct.

A. I understand that's when they published it, but they haven't updated the reference list of meta-analysis like Penninkilampi.

Q. The document we're looking at states in terms of the date it was updated is May 30th, 2019. We can agree on that. Right?

A. Yes, but they failed to include up-to-date references and analysis of the issues related to talcum powder and ovarian cancer.

Q. And what this document that we have been reviewing from the NIH, NCI concludes is that the weight of the evidence does not support an association between perineal talc exposure and an increased risk of ovarian cancer. Correct?

A. Based on inadequate evaluation, I've shown you data today from references that are more up to date that the NCI has apparently chosen or not been complete in their evaluation of the topic that we're talking about.

Q. I want to take a closer look at some of the data the NCI did review. But as to the NCI's review of the evidence that they state was updated in May, again, that's not a process that you personally took part in. Correct?

A. I was not involved with this, no.

Q. So you don't know the decision-making of the scientists and professionals at NCI that went into their determination that the weight of the evidence does not support an association between perineal talc exposure and an increased risk of ovarian cancer. True?

A. I don't know their process or who was involved in any of that, no.
Q. Now, let's take a look at page 12, and if we can blow up that so we have it.
That first paragraph starts:
"The discussion of the scientific data on perineal talc exposure and ovarian cancer." And what the scientists at the NIH state is that "the results from case control and cohort studies are inconsistent."
Do you see that?
A. Yes.
Q. And it goes on to talk about a pooled analysis from the Ovarian Cancer Association Consortium. Do you see that?
A. Yes.
Q. You know what that is. Right?
A. Yes.
Q. That's the Terry analysis on which you rely. Correct?
A. That's one of the many papers that we considered as you got my analysis.
Q. And, in fact, the reason -- one of the reasons you cite the Terry paper in your expert report is for the proposition that it showed a dose-response. Do

you recall doing that?
A. Possibly. There are several others as well, and this Terry report shows a statistically significant increased risk of ovarian cancer, 24 percent, right there on the bottom line.
Q. When it comes to the score of dose-response, the reason that you cited the Terry analysis -- let's take a look at what the scientists at this government health organization said.
Now, they said that this Terry study found a modest increased risk of epithelial ovarian cancer --
A. Statistically significant increase, yes.
Q. Is it important, Doctor, that it's statistically significant?
A. It's one of the important things. Relative risk is also important. Relative risk is increased by 24 percent.
Q. But in terms of evaluating a scientific study, you, as a doctor, as a gynecologic oncologist, it is important to you that that confidence interval shows statistical significance. Is that right?
A. That's not the only thing. Weight of the evidence is what's important.
Q. What these scientists say is "but the trend across increasing lifetime number of applications was

not statistically significant."

Do you see that?

A. Yes. I'm trying to look at the references they are using. The first one reference 43 was from 2003, which is out of date. Terry was 2013. There are other references that I've included in my report that talk about dose-response. So they've cherry-picked or they are just out of date with their references.

Q. To focus you for a second, Dr. Clarke-Pearson, I want to talk about the Terry analysis from 2013. Are you with me?

A. I'm with you.

Q. That is end note 44. Right?

A. Yes, for reference, 43.

Q. You and I can agree you cited this study in your report for the proposition that it showed a dose-response. Correct?

A. Along with others. The totality is what I have been looking at as I make my analysis, not one paper or report over another.

Q. And what these government scientists state in this document, concluding that there is inadequate evidence of an association, what they say about the Terry tape is that "increasing lifetime number of applications was not statistically significant."

Correct?
A. That's what that says, and there are other papers that say that it is.
Q. And one of the studies you spoke with us about this morning, Doctor, was the Schildkraut study. Do you remember that?
A. Yes.
Q. That was a study from 2016. Correct?
A. Right.
Q. These folks in fact go on to talk about it, correct, case-control studies of African-American women in the United States. Do you see that?
A. Yes.
Q. And they go on to talk additionally about the Women's Health Initiative prospective study. Correct?
A. Yes. One of the cohort studies. The Schildkraut study showed a 44 percent increased risk of ovarian cancer.
Q. When considering all of the evidence, they came to the conclusion that perineal talc exposure was not adequate to support a risk for ovarian cancer. Correct?
A. Could you read back what she just said.
Q. What the scientists at the NIH concluded is that there is inadequate evidence of an association between

perineal talc exposure and ovarian cancer. Correct?
A. They didn't consider all the evidence. The evidence that they had, they can say that, but they didn't consider all the evidence.
Q. Doctor, the document said it was updated two months ago?
A. How come they didn't include references that are more updated?
Q. You don't have any personal knowledge why they did or did not include any of the references here; do you?
A. No, I don't. It's disappointing the National Cancer Institute can't publish something that's more up to date.
Q. I want to talk a little bit, Doctor, about the FDA. You know, of course, in addition to ACOG to some of the other organizations we've look at, the FDA has also had an opportunity to review data on the alleged association between perineal talc exposure and ovarian cancer. Correct?
A. I'm not aware of what they published.
Q. We talked about this a little bit in your deposition. Right? You know the FDA received something called a citizen's petition. You are familiar with that?

A. I'm aware of that letter, yes.
Q. Let's take a look at that letter which is 506 in your binder.
Doctor, you are familiar generally with the process of a citizen's petition. Correct?
A. You have to explain that to me.
Q. You have seen, at least in connection with your expert work for the plaintiffs in this lawsuit, you have seen at least the documentation from the FDA responding to a citizen's petition requesting an ovarian cancer warning on talcum powder products?
A. I'm aware of that. I don't know the whole process.
Q. I want to talk about the FDA's review of the scientific data and their conclusions about whether or not talcum powder causes ovarian cancer?
Now, this document is from 2014. Correct?
A. Yes.
Q. And as we just discussed, the FDA is responding to a petition requesting that talcum powder products have a warning regarding the risk of ovarian cancer. Right?
A. Yes.
Q. And what the FDA concluded is that "after careful review and consideration of the information

submitted in your petitions, the comments received in response to the petitions, and review of additional scientific information, this letter is to advise you that the FDA is denying your petitions."

Right?

A. That's what it says.

Q. And what the FDA concluded is that the FDA did not find that the data submitted presented conclusive evidence of a causal association between talc use in the perineal area and ovarian cancer. Right?

A. I don't know what data was submitted, and I don't know what the analysis of the FDA was. This organization submitted a petition in 1994 and then again in 2008, and the FDA finally responded in 2014. I'm not quite sure what the process is that you are alluding to, but it doesn't sound very timely, and the FDA doesn't reference any references whatsoever here. To me this is not a publication. It's a letter denying this petition.

Q. Let's talk about what we do know, what's contained in this letter. Are you with me?

A. I'm with you.

Q. We do know this is a document from the Food & Drug Administration in 2014. Right?

A. Right, in response to a letter from 1994.

Q. And 2008. See that?
A. Right.
Q. What we do know, what the FDA states in this document, is that the FDA did not find that the data submitted presented conclusive evidence of a causal association between talc use in the perineal area and ovarian cancer --
A. That's what this says.
Q. You are not aware of any other proclamation or publication or document from the FDA that would suggest that it has found a causal association between talc and ovarian cancer?
A. I'm not aware of any documentation from the FDA evaluating talcum powder whatsoever.
Q. Let's look at some of the details of the FDA's evaluation in this document.

One of the pieces of information that the FDA reviewed in connection with this document is found on page 3, and it relates to the 1993 National Toxicology Program report. Do you see that?
A. Yes.
Q. Doctor, in fact, you cite that 1993 toxicology report in your expert report in this case. Correct?
A. Yes, for a different reason.
Q. You cite the 1993 NTP study in your report

following the sentence that says:

"Talcum powder is known to elicit an inflammatory response in animals and humans."

Correct?

A. Yes, continuing my belief that chronic inflammation caused by talcum powder results in ovarian cancer.

Q. And just to orient us, let me put it up on the screen so you and I are on the same page here.

This is your report in this case. In the section entitled "Inflammation and cancer," you state:

"Talcum powder is known to elicit an inflammatory response in animals and humans."

And you have three cites there. Right?

A. Yes.

Q. And one of them is this 1993 NTP study. Right?

A. Yes, which demonstrates inflammation caused by talcum powder.

Q. And you know the FDA made some conclusions after it had the chance to review this 1993 NTP study. Correct?

A. Right.

Q. And what the FDA included, included some of those criticisms in this 2014 letter. Correct?

A. Yes.

Q. And what the FDA concluded was that this 1993 NTP study lacks convincing scientific support because of serious flaws in its design and conduct. Correct?
A. That's what the FDA is interpreting that.
Q. One of the flaws the FDA identified was that the investigators used micronized talc instead of consumer grade talc. See that?
A. That was one of their criticisms.
Q. From the FDA's view that resulted in the experimental protocol not being reflective of human exposure conditions in terms of particle size. Do you see that?
A. I see that micronized talc is part of it, but it is not the consumer grade talc. I agree with you on that type.
Q. Do you understand there to be a difference between micronized talc and the talc particles in consumer grade talc?
A. Yes.
Q. You didn't mean to suggest they are the same thing?
A. No.
Q. Another critique that the FDA had, was of this study on which you rely in your report was that the investigators conceded that they had problems with the

aerosol generation system. Do you see that?
A. Yes.
Q. And a final critique the FDA notes here is that the study did not include positive and negative dust controls which would have permitted an exact assessment of the talc's carcinogenicity relative to the two control dusts. Do you see that?
A. This study wasn't designed to look at carcinogenicity. It was designed to look at chronic inflammation.
Q. And what the scientists at the FDA concluded is that in light of all of those shortcomings, there was a panel of experts at an FDA workshop that declared this study on which you rely had no relevance to human risk. Do you see that?
A. Yes.
Q. And one of the other things the FDA did in connection with the review of this request from a citizen to label cosmetic talc with an ovarian cancer warning is they reviewed the epidemiology. Right?
A. That's what they say they did, yes.
Q. And one of the things that the scientists at the FDA determined, based on their review of the epidemiology, is that a dose-response evidence is lacking. Do you see that?

A. Yes. So, obviously, they didn't read the literature that does show dose-response.
Q. And to be clear, Doctor, the FDA's conclusion on dose-response, that is different than yours. True?
A. Yes. They don't even cite what references they looked at to come to that conclusion.
Q. You disagree with the FDA's conclusion that the epidemiology does not show a dose-response. Correct?
A. I disagree, yes.
Q. And you know, of course, that Health Canada, they found the same thing. Right?
A. I didn't find a dose response. I would have to look at that manuscript again.
Q. We can take a look at it later. If true, you would disagree with that as well?
A. Yes.
Q. Another thing the FDA found in reviewing the epidemiology is that a cogent biological mechanism by which talc might lead to ovarian cancer is lacking. Do you see that?
A. I see that. In 2014 it was becoming quite clear in the oncologic community that chronic inflammation causes cancer. So I guess the FDA missed those review articles or primary articles.
Q. I want to talk in depth, what you are relying

on, that a cogent biological mechanism has in fact been established. Before we do that, is it fair to say you disagree with the FDA on this score? Correct?

A. Yes, I did.

Q. You believe that a cogent biological mechanism has been established. Right?

A. Yes.

Q. And you believe that mechanism is inflammation?

A. Chronic inflammation, yes.

MS. BROWN: Your Honor, I don't know if this is an appropriate spot to stop.

THE COURT: We'll break now and be back in 45 minutes.

MS. BROWN: Thank you, your Honor.

THE DEPUTY CLERK: All rise.

(The luncheon recess is taken.)

(Continued on the next page.)

///

A F T E R N O O N S E S S I O N

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

DANIEL CLARKE-PEARSON, resumed

CROSS-EXAMINATION (Continued)

BY MS. BROWN:

Q. Welcome back, Dr. Clarke-Pearson.

A. Good afternoon.

Q. Just to orient us as to where we were before we took the lunch break, we were talking about the 2014 FDA letter. Do you recall that?

A. Yes.

Q. In fact, you and plaintiffs' counsel cited the 2014 FDA letter in your presentation to the Court this morning. Correct?

A. Yes, for different reasons.

Q. You cited part but not all of this FDA letter. Correct?

A. Yes.

Q. You agree with part but not all of the FDA's findings in 2014?

A. The point of the FDA was there was a reasonable

understanding on their part that migration was something they believed in and supported.

Q. And as it relates to the FDA's ultimate conclusion that a causal association between talc use in the perineal area and ovarian cancer had not been established. You disagree on that score. Correct?

A. Yes, ma'am.

Q. We were talking about the FDA's finding that a cogent biological mechanism by which talc might lead to ovarian cancer was lacking. Do you recall that?

A. I see that, yes.

Q. The truth, Dr. Clarke-Pearson, is that no one knows for sure how ovarian cancer develops. Would you agree?

A. I think there is mounting evidence and strong evidence that in the case of talcum powder, it's chronic inflammation that sets off the whole cascade that results in cancer.

MS. BROWN: Permission to read, your Honor?

THE COURT: Yes.

Q. Let's go to your deposition from February 4th, and I would like to take a look at page 91, lines 19 through 23. At your deposition you were asked:

"QUESTION: Is it true that no one knows for sure how ovarian cancer develops?"

There was an objection.

"ANSWER: I guess no one knows for sure."

Correct?

A. Yes.

Q. One of the things you spoke to us about this morning was the hypothesis that incessant ovulation leads to inflammation. Do you recall that testimony?

A. That's not a hypothesis. It seems to be well-established in many studies for many years. Incessant ovulation and inflammation, yes.

Q. And in support of that testimony you showed the Court an article by Shan and Liu. Do you remember that?

A. I'll have to see it again.

Q. Do you recall discussing this article this morning?

A. Yes.

Q. This is a review article from 2009. Correct?

A. Yes.

Q. That's five years before you were on Fox News identifying risk factors. Correct?

A. Yes.

Q. And one of the things -- and this review article does not include new in vitro or in vivo research. Correct?

A. I would have to look at the references to see what's new in the article or not.
Q. Well, you presented this as part of your direct examination. Do you remember that?
A. Yes.
Q. You would agree with me it's a review article. Right?
A. Yes.
Q. It is summarizing the state of science according to these authors at the time. Correct?
A. Okay. Up to that time.
Q. I think the ELMO is somehow broken.

MS. BROWN: One moment, your Honor.

(Pause.)

Q. This review article from 2009 that you spoke about this morning reports that:

"In an effort to identify the causes of epithelial ovarian cancer a few hypotheses have been put forward."

Do you see that?

A. Yes.
Q. And one of the theories or hypotheses that this article that you spoke about this morning discusses is the incessant ovulation hypotheses. Right?
A. Yes.

Q. And it goes on to identify two additional theories or hypotheses. Correct?
A. Yes.
Q. And, in fact, when you referred to the incessant ovulation potential mechanism in your report, you, too, referred to it as a theory. Correct?
A. Okay.
Q. Do you agree with me?
A. Yes.
Q. In fact, you reported that there are several theories as to the origin of ovarian cancer. Correct?
A. Yes.
Q. And you know that the hypothesis that ovarian cancer could be caused by inflammation is something that has been studied for a while now. Correct?
A. Yes.
Q. And one of the articles in fact that you have on your reliance list is a paper by the author Melissa Merritt?
MS. BROWN: For the record, it's Exhibit 511.
Q. Now, this is a 2007 article by Melissa Merritt entitled, "Talcum Powder Chronic Pelvic Inflammation and NSAIDs in Relation to the Risk of Epithelial Ovarian Cancer."
Do you see that?

A. Yes.
Q. This is one of the articles you reviewed in connection with the opinion you gave to this Court this morning. This was actually an epidemiologic study investigating the potential mechanism of chronic inflammation in causing ovarian cancer. Right?
A. Yes.
Q. And what the authors state is that "chronic inflammation has been proposed as the possible causal mechanism that explains the observed association between certain risk factors such as talc."
Do you see that?
A. Yes.
Q. And what they conclude is that "chronic inflammation does not play a major role in the development of ovarian cancer."
Do you see that?
A. Yes.
Q. That's based on some of the results conducted in this study in 2007. Right?
A. Yes.
Q. And what the authors of the Merritt study note back in 2007 is that until the present study, no other epidemiological studies appear to have tested the hypothesis that ovarian inflammation is associated

with ovarian cancer risk. Do you see that?
A. Yes.
Q. What they go on to report in the study is a number of results that support their conclusion that chronic inflammation is unlikely to play a role in the development of ovarian cancer. And one of those findings relate to something called pelvic inflammatory disease. Do you see that over here, Doctor?
A. I do.
Q. Pelvic inflammatory disease is one of the inflammatory conditions you spoke to the Court about this morning. Do you remember that?
A. Yes.
Q. What the authors of the Merritt study say in 2007 is that if inflammation plays a role in the etiology of ovarian cancer, it would be expected that PID, or pelvic inflammatory disease would be associated with an increased risk of cancer. See that?
A. I see that. There are two types of pelvic inflammatory disease. Those that are acute and treated with antibiotics and others that are chronic.
Q. Do you see that sentence from the Merritt study?
A. Yes.

Q. One of the things the investigators were looking at was whether inflammatory conditions were at all related to the risk of ovarian cancer. Right?
A. I understand.
Q. Because if your theory is that chronic inflammation causes ovarian cancer, you will expect to see an association between inflammatory conditions like PID and ovarian cancer. Right?
A. In chronic pelvic inflammatory disease, yes.
Q. That's exactly what these investigators were trying to get to the bottom of in this epidemiology study that you reviewed in connection with your opinions?
A. There are other studies that support that PID is a risk factor for ovarian cancer.
Q. I want to talk about those. Let's focus on this paragraph here and get through this article.

What these investigators found in the Merritt paper you reviewed was that PID was not associated with elevated risk of ovarian tumors in our data confirming several previous reports of no association with PID in studies of all subtypes of ovarian cancer. Do you see that?
A. I see that.
Q. Another thing that these investigators looked at

was NSAIDs. Do you recall that?
A. Yes.
Q. The theory there being that, in fact, if it is true that ovarian cancer is caused by an inflammatory response, then an anti-inflammatory medication like NSAIDs should reduce the risk. Right?
A. It depends what NSAIDs you study.
Q. That's a theory. Right?
A. Theory.
Q. These investigators looked into this, and this is what they found:

"If inflammation did promote epithelial ovarian cancer development, then it may be reasonably expected that regular use of anti-inflammatory medications would reduce risk. However, no overall association with ovarian cancer risk was observed in the study."

Correct?
A. There are other studies that show use of long-term aspirin does reduce the risk.
Q. My question was directed to that paragraph.
A. This one paper in this one paragraph, I agree what you read to me.
Q. I'm going to talk about some of the other studies you showed this morning to the Court in

support of your opinion that ovarian cancer is caused by inflammation, but I want to start just with this Merritt paper.

What these investigators found was that there was no association observed between people taking anti-inflammatories, and they did not see a connection. Correct?

A. That's correct.

Q. That led them to conclude that chronic inflammation is unlikely to be a cause of ovarian cancer. Correct?

A. That's their conclusion, yes.

Q. This was back in 2007 right, Doctor?

A. Yes.

Q. And this theory that ovarian cancer may be caused by inflammation, it has continued to be studied. Correct?

A. Yes.

Q. One of the studies that you showed this morning in connection with your opinion that talc produces a chronic inflammation that leads to cancer, one of the studies you showed the Court this morning was the Penninkilampi study. Do you remember that?

A. Yes.

Q. And I got a set of the slides that you guys were

going to use this morning. But when you did a call-out from the Penninkilampi slide, that wasn't in my prepared deck. So what I did was I highlighted what you guys had on the screen and I want to talk to you about it. Okay?

You spoke about Penninkilampi supporting a chronic inflammatory mechanism. Do you remember that?

A. Yes.

Q. And what you guys had up on the screen is what I've highlighted in pink. Do you see that?

A. Yes.

Q. It was sort of cut-and-paste. You had the paragraph on the left, and there was a little space, and you had that one sentence on the right. Did you pick the sentences from Penninkilampi to put up?

A. We had some points to make like you are making.

Q. So you put that slide together?

A. With the assistance --

MS. O'DELL: It wasn't a slide, as you know.

MS. BROWN: You did it on the fly.

MS. O'DELL: Yes.

BY MS. BROWN:

Q. I want to talk to you about what you and counsel did on the fly as it relates to what you told the Court Penninkilampi stood for, and I want to talk

about whether that really fits with what this article says.

So you put up what's in pink, that it's been proposed that talc may ascend from the vagina to the uterine tubes and create an inflammatory response. Do you see that?

A. Yes.

Q. You left out the sentence above it that says:

"The mechanism by which perineal talc use may increase the risk of ovarian cancer is uncertain."

Right?

A. Yes.

Q. This is the 2018 meta-analysis on which you rely in your report. Correct?

A. Yes.

Q. And what the authors of this study found is that the mechanism is uncertain in 2018. Correct?

A. Yes.

Q. And what they go on in the parts that were not put up during your direct examination is they talk about some of the reasons that the mechanism remains unclear; do they not?

Do they not go on to talk about the proposed hypothesis and some of the evidence in relation to that hypothesis?

A. Yes. In this discussion. The meta-analysis was not -- this is all their discussion that goes on beyond what the findings were in the meta-analysis.

Q. And what they state is that it's been previously proposed that talc may instigate a chronic inflammatory response. That's the part you showed the Court. Right?

A. That's part of their discussions.

Q. In support of their hypothesis, "It's been found hysterectomy or bilateral tubal ligation in which ovarian exposure to inflammatory mediators would be significantly curtailed is associated with the increased risk of ovarian cancer."

Correct?

A. Yes, that's what is referenced there.

Q. What they go on to say is that:

"However, the use of non-steroidal anti-inflammatory drugs is not inversely associated with the incidence of ovarian cancer as may be expected if an etiology was related to chronic inflammation"?

A. Could you let me take a look at the two references here?

Q. It's A 109, and I want to talk about the part of this article that you showed the Court this morning

that stood for the proposition that Penninkilampi -- that chronic inflammation is an established mechanism. And the sentence I just read there, Doctor, states that NSAIDs have not been inversely associated with the incidence of ovarian cancer as would be expected if chronic inflammation causes ovarian cancer. Right?

A. These two references, one of which is Merritt, which you already went through, and there are other references that show that the use of aspirin on a continuous daily basis does reduce the incidence of ovarian cancer.

Q. Some of those studies are very recent; aren't they?

A. I can't remember when they were published. There is evidence today, as we sit here in this courtroom trying to evaluate the current evidence, that aspirin does reduce the risk of ovarian cancer.

Q. And one of the things that folks that have written those aspirin articles, scratching their head about this chronic inflammation hypothesis is that those very same studies that have shown a low dose aspirin to be protective have not found any protection with NSAIDs. Right?

A. Aspirin is a non-steroidal anti-inflammatory.

Q. Do you know the study I'm talking about, Doctor?

A. Remind me.
Q. We'll take a look at it in a minute. You know there have been inconsistent findings on whether or not NSAIDs and aspirin in fact reduce the risk of ovarian cancer. Right?
A. There are some that are positive.
Q. And what this study that you put up this morning and said, suggested that chronic inflammation was the mechanism by which talc causes ovarian cancer, what this study actually concludes is that the potential mechanism by which genital talc is associated with an increased risk of cancer, hence remains unclear. Right?
A. So this study by Penninkilampi is not looking at that issue. This is their discussion. What they have is a meta-analysis looking at the risk of developing ovarian cancer, being exposed to talcum powder. So this is all part of their discussion about the outcomes of their study and why things might have happened the way they are. This is not the intent of the study, to talk about anti-inflammatories or chronic inflammation.
Q. And when you put your presentation to the Court together, you highlighted what I have highlighted in pink. Correct?

A. That's correct.
Q. And you testified that Penninkilampi showed that chronic inflammation from talc causes ovarian cancer. Right?
A. I don't recall testifying that it showed it, but that there are other papers that do show chronic inflammation as causing ovarian cancer and other cancers.
Q. And what this article actually says is that the mechanism by which perineal talc use may increase the risk of ovarian cancer is uncertain. Correct?
A. That's what they are saying, that's correct.
Q. And what they actually say in this article, is that NSAIDs findings have not supported the chronic inflammation theory. Right?
A. With two references, and there are other references one could use.
Q. And what they actually said is that the Cox-2 study has not supported the mechanism. Right. Correct?
A. That's what it says right there.
Q. This Penninkilampi article does not support the hypothesis that chronic inflammation causes ovarian cancer?
A. The paper is a meta-analysis supporting the

finding that use of endometrial talc increases the risk statistically of ovarian cancer.

Q. This is one of the most recent meta-analyses on which you rely. Correct?

A. Yes.

Q. This is one of the most recent meta-analyses that has been done at all on the topic of talc and ovarian cancer. Correct?

A. Yes.

Q. And you put this article up this morning for two propositions: one that it showed chronic inflammation causes ovarian cancer. Correct?

A. In their discussion, yes.

Q. And that is not at all what this article says. Right?

A. I think it does -- I need to speak to the Court, if I can. In a scientific peer-reviewed paper, a discussion does not necessarily discuss everything that's in the paper. It can expand on this and become more global, and that's what they are doing in this discussion that we are going back and forth in yellow and pink.

THE COURT: Okay. Let's see if you can answer the question counsel just asked.

MS. BROWN: Thank you, your Honor.

Q. This article does not state that the chronic inflammation is the mechanism by which talc causes ovarian cancer?

A. Right, that was not the intent of this article. This is a meta-analysis looking at risk.

Q. If we go back to the transcript and we see a suggestion that you said otherwise, that would be mistaken?

A. I'm not quite sure I understand what you are saying.

Q. You also used this article this morning to suggest that it proves that talc causes ovarian cancer. True?

A. Yes.

Q. Let's talk about whether what the authors actually say fit the opinion that you gave on that score. Okay?

A. Okay.

Q. (Reading.)

"The evidence for the association between perineal talc use and ovarian cancer is based on the body of knowledge from observable studies, and most of these have been retrospective case-control studies prone to recall bias?"

Do you see that?

A. I do.
Q. (Reading.)
"Hence, while perineal talc use has not been shown to be safe in a similar regard, a certain causal link between talc use and ovarian cancer has not yet been established."
Do you see that?
A. I do. This is in the introduction to their paper explaining why they undertook this meta-analysis.
Q. The authors of the Penninkilampi paper state that a causal link has not been established. Do you see that?
A. This is in the introduction to the paper before they did their study and reported their results. They are explaining why they did the study because they felt a causal link hadn't been established, they did their meta-analysis, and now we have a relative risk that's statistically significant.
Q. This paper did not conclude that talcum powder causes ovarian cancer. True?
A. This paper shows a significantly elevated risk of the use of talcum powder and the occurrence of ovarian cancer. So I think it says it causes ovarian cancer.

Q. Nowhere in this paper does it state that talcum powder causes ovarian cancer?
A. I would have to look at the words throughout the whole paper and look for cause. I can see what the relative risk is. I could see what the statistical risk is, and it increased significantly.
Q. This is one of the six meta-analyses on which you rely. True?
A. And all of them showed significant increase risk of ovarian cancer with the use of perineal talc.
Q. And this says a causal link has not been established?
A. That's in their introduction, yes.
Q. What this article says is a mechanism remains unclear. Correct?
A. That's what is in their introduction.
Q. And another meta-analysis that was done in 2018 was the Berge analysis. Correct?
A. Yes.
Q. And incidentally, Doctor, one of the things your methodology here was to rely on the meta-analyses. Correct?
A. In the end, my methodology evaluated all the case-control, cohort and one pooled study, and the meta-analysis. The meta-analysis I feel are more

powerful because they include many more studies.
Q. What you tell us in your report is that while recent case-control studies and cohort studies are compelling, you feel meta-analysis studies, because they include larger numbers of patients, results in a greater statistical power. Right? That's what you said in your report.
A. Okay. If it says it in the report, yes.
Q. You wrote it, right?
A. I'm trying to find it.
Q. It's on the screen right at the top. Are you with me?
A. Yes.
Q. So these are your words in your report, that while case control and cohort studies are compelling, you feel that meta-analyses are much stronger. Right?
A. Yes.
Q. Those are the words you wrote in your expert report here. Right?
A. Yes.
Q. And then you created a chart of a number of pooled analyses or meta-analyses. Correct?
A. And I failed to have one on there, which is Berge.
Q. We spoke about Penninkilampi. That found the

mechanism is uncertain. Right?
A. That's what they say in their discussion.
Q. And another 2018 meta-analysis that you left off of the list was the Berge meta-analysis. Right?
A. Yes.
Q. What was your methodology for creating this list and how did Berge get left off?
A. It was clearly an oversight on my part. I'll admit to human error.
Q. And what the authors of the Berge 2018 meta-analysis find on this issue of biological plausibility is that the biological basis and plausibility of a possible carcinogenic effect of talc on the ovaries is still not understood and remains questionable. Right?
A. Again, in their discussion it wasn't the intent of this meta-analysis to determine the plausibility of what the carcinogenic effect was.
Q. What the authors of the Berge 2018 meta-analysis found is that the mechanism by which talc could cause ovarian cancer is not understood and remains questionable. Right?
A. It didn't find that in this study.
Q. Those are the words in the study on the page that we're looking at. Right?

A. It didn't say that they found it.
Q. The opinion of the authors as documented in the peer-reviewed literature in a meta-analysis that you neglected to put in your report is that the biological basis and plausibility of a possible carcinogenic effect of talc on the ovaries is still not understood and remains questionable. Correct?
A. Yes. It's not that they found that. They didn't find that. That's just their opinion.
Q. And what the authors who conducted this meta-analysis say in conclusion is that several aspects of our results, including the heterogeneity of results between case-control and cohort studies, do not support a causal interpretation of the association. Do you see that?
A. I see that.
Q. That is the conclusion of the authors of the meta-analysis that was omitted from your report. Correct?
A. Right. I failed to put it in the report.
Q. You would agree that research regarding whether chronic inflammation can cause ovarian cancer is ongoing. Correct?
A. Yes.
Q. And that the inflammation hypothesis is still

being studied in laboratories. Correct?
A. Yes.
Q. And as Her Honor asked you about earlier this morning, none of those studies show that when you put talc on a cell, cancerous changes occur. Right?
A. Right. The precursors of cancer have been identified. No cancer has been seen in a cell culture or laboratory.
Q. And you are relying on that for your opinion in part on the work of Dr. Saed. Correct?
A. And several others.
THE COURT: Which other ones?
THE WITNESS: Shukla, Buz'Zard, Akhtar, two papers.
Q. And you, Doctor, do not know how much talcum powder a product must contain to cause inflammation. Correct?
A. You are saying the minimum amount?
Q. How much? How much talcum powder causes inflammation. You don't know the answer to that. Correct?
A. Inflammation in some of these in vitro studies has been induced by talcum powder. The dose the investigators used in some of these studies resulted in inflammation.

Q. You are not aware of a certain amount of talcum powder that a product must contain to cause inflammation. Correct?
A. Maybe I'm trying to paraphrase you, that I should know the minimum amount that would cause inflammation? Could you rephrase your question.
Q. Let's just look at your testimony on this score from your deposition, page 223, lines 24, to 224, line 1:
"QUESTION: Is there a certain amount of talcum powder that a product must contain to cause inflammation?
"ANSWER: We don't know that information."
Correct?
A. That's correct, and that would still be my answer.
Q. You do not believe, Doctor, that there exists a threshold amount below which a woman exposed to talcum powder is not at an increased risk of developing ovarian cancer?
A. Could you say that again.
Q. You do not believe there is a threshold amount below which a woman exposed to talcum powder is not at risk for developing ovarian cancer?
A. Yes, we don't know.

Q. You do not have an opinion there is a safe level of exposure to talcum powder. Correct?
A. No, but we know the dose-response in the studies that have looked at dose response show the increased risk with increasing dose.
Q. You do not think that there is a threshold amount below which exposure to talcum powder is safe?
A. I don't know that threshold, no.
Q. You have not identified how much talcum powder must reach a woman's ovaries for her to undergo chronic inflammation that leads to cancer. Correct?
A. That's correct.
Q. And in your opinion, because we don't know that information, any amount of talcum powder that a woman uses can cause ovarian cancer. Right?
A. I think it increases the risk of causing ovarian cancer, yes.
Q. You have not endeavored in this case to identify a threshold dose of talcum powder below which you do not believe ovarian cancer can be caused. Correct?
A. That's correct.
Q. And what that means, Doctor, is that, for example, if a product contained 1 percent talcum powder and 99 percent cornstarch, in your opinion, that product could cause inflammation resulting in

ovarian cancer. Correct?
A. If the talcum powder was the same as Johnson & Johnson's Baby Powder or Shower To Shower that was included with the cornstarch hypothesis that you have thrown out, then I would say that, yes -- I would answer your question yes.
Q. Are your opinions in this case limited to only Johnson & Johnson talcum powder products?
A. No, but since they have the market share and most of the studies in epidemiology, those women were using these products, that's where I stand.
Q. But in answering my question about a hypothetical product with 1 percent talc, I thought I heard you to say if that 1 percent talc was J&J talc. Did I misunderstand you?
A. It depends on what you mean by talc. Is it talcum powder J&J makes? Is it pure powder? Does that talc have heavy metals, asbestos and fiber in it?
Q. I'm going to take J&J out of this completely. If you have a hypothetical product with 1 percent talc and 99 percent cornstarch, in your opinion that product can cause ovarian cancer. True?
A. If that product had the same composition as Johnson & Johnson's, then I would say true.
Q. Your opinion, though, when you say that is not

dependent on the Johnson & Johnson products containing, for example, heavy metals. Correct?
A. It's the entire product.
Q. If the Johnson & Johnson products did not contain heavy metals, you are still of the opinion they cause ovarian cancer. True?
A. Yes.
Q. If the Johnson & Johnson products do not contain asbestos, you are still of the opinion that they cause ovarian cancer. True?
A. I'm saying the Johnson & Johnson products cause ovarian cancer, whatever is in it.
Q. And you cannot cite to any published study that supports your opinion that any amount of talc a woman uses perineally leads to chronic inflammation. Correct?
A. That's correct.
Q. The truth is, Doctor, not all inflammatory conditions lead to cancer. True?
A. True.
Q. There are conditions that cause acute inflammatory reactions purposely. Right?
A. Yes.
Q. Pleurodesis is one of those procedures. Correct?

A. Yes.
Q. So pleurodesis is a procedure by which talc is injected into the pleural space of a patient. Right?
A. Like we discussed this morning, yes.
Q. And the purpose of doing that is to create an acute inflammatory response. Right?
A. Yes.
Q. And the idea is that the talc will absorb the fluid and allow the person to breathe easier. Correct?
A. The talc doesn't absorb the fluid. The talc causes scarring between the lung and the chest wall by way of an inflammatory response.
Q. And one of the things the scientists at IARC did was they looked at people who had undergone pleurodesis for a number of decades to see if they developed cancer. Right?
A. I would have to see the studies.
Q. Did you review IARC's conclusion on whether or not folks who had pleurodesis got cancer in connection with your opinions here?
A. I would have to refresh my memory on that.
Q. You wouldn't expect somebody who underwent pleurodesis and had acute inflammatory response would develop cancer. Right?

A. I have two parts to that answer.

One, you are talking about acute inflammatory response. I've been talking about chronic inflammatory response.

No. 2, the majority of men and women that have pleurodesis have malignant pleural effusions and don't survive long enough to find out whether or not the talc might also cause the cancer.

Q. Doctor, you are not familiar with the standard of care as it relates to the use of pleurodesis. Is that fair?

A. I use pleurodesis in my practice on thankfully not a daily basis, but several times a year with women who have malignant pleural effusions.

Q. Are you aware of the indication of pleurodesis for people with benign lung conditions?

A. Yes. It is used for that condition too, called pneumothorax, not benign. It's one lung condition.

Q. You are aware pleurodesis is used for people who do not have cancer?

A. Yes.

Q. I want to talk a little bit, Doctor, about IARC. You are, of course, familiar with IARC's review of the epidemiology regarding talc and ovarian cancer. Correct?

A. Yes.
Q. And you know and I can direct you -- if you want a copy, we have one here for you. It is 510-A 70. I'm sorry.
(Pause.)
Doctor, we are now looking at A 72, which is the IARC monograph on talc that you reviewed in connection with your opinions here. Correct?
A. Yes.
Q. I want to direct your attention to page 423 where the IARC scientists give their evaluation and rationale for their classification of perineal use of talc. You reviewed this. Correct?
A. Yes.
Q. You know IARC has not concluded that talc causes ovarian cancer. Correct?
A. This is a 2010 publication based on data that preceded the working group coming to this conclusion.
Q. One of the things, Doctor -- let's pause there and talk -- first, we can agree at the time of this publication IARC did not conclude, as you have done here, that talc causes ovarian cancer. Right?
A. Yes.
Q. And you raise a question about what was available to IARC at the time that they did this

review that was published in 2010. Is that right?
A. What was the question?
Q. I thought you were just raising an issue what IARC would have had available at the time of this review. Are you with me?
A. I was trying to read the report at the same time you were asking the questions.
Q. One of the things IARC would not have had at the time of this review is the 2014 Prospective Woman's Health Initiative Study. Correct?
A. They wouldn't have had many of the studies.
Q. One of the things would have been one of the cohort studies. Right?
A. Yes.
Q. And you know that in 2014 there was a prospective cohort done as part of the Women's Health Initiative. Right?
A. Yes.
Q. And that study did not find an increased risk of ovarian cancer with the use of talc. Correct?
A. It showed an increased risk, yes.
Q. That study did not find a statistically significant increased risk of ovarian cancer with talc use. Correct?
A. It showed an increased relative but not a

statistically increased risk.
Q. The scientists who conducted the WHI prospective study did not find a statistically significant increased risk of ovarian cancer with perineal use of talc. Correct?
A. In that one cohort study, among several cohort studies, and among 20 some odd case-control studies.
Q. The answer to my question is "yes." Right?
A. The question was, it didn't find an association --
Q. Let's do it again.
In 2014 the investigators at the Women's Health Initiative conducted a study in which they did not find a statistically significant increased risk of ovarian cancer from talcum powder use. Correct?
A. Relative risk was increased but not statistically.
Q. And that prospective cohort would not have been available to the IARC investigators that did this review. Correct?
A. That's true, and I think probably other studies too. I would have to look at the dates of other studies we have been talking about today.
Q. Another prospective cohort study that would not have been available to the investigators doing the

IARC review back in 2010 is the Gonzalez study. Correct?

A. Yes, the Sister Study.

Q. And that study also did not find a statistically significant increased risk of ovarian cancer with talc use. Correct?

A. The relative risk was increased but not statistically. The study has many problems with it. Trying to dissect one study in the totality of the literature we have to look at is, I think, not appropriate.

Q. I want to make sure I don't run over my time and I get you out of here, so I'll appreciate it if you listen to my question.

That study did not find an increased risk of ovarian cancer with perineal talc use. True?

A. That's true.

Q. And that study would not have been available to the investigators who conducted this IARC review. Correct?

A. That's correct.

Q. In 2010, the Gates study followed up on the prospective cohort that was followed in the Gertig study. Correct?

A. Yes.

Q. And when the Gates investigators followed up, they did not find a statistically significant increased risk of ovarian cancer with perineal talc use. Correct?
A. Increased relative risk but not statistically significant increased risk.
Q. And that, too, would not have been available to the scientists conducting the IARC review in 2010. Correct?
A. That's correct, along with other case-control studies that were not available at the time.
Q. There are a total of three case control-studies on the issue of talc and ovarian cancer. Correct?
A. Three case control-studies?
Q. I misspoke. Three cohort studies. Correct?
A. Yes.
Q. And the Gertig, the original Gertig study has a cohort that was followed up in 2010. Right?
A. Yes, the Nurses' study.
Q. In terms of what the folks do in this review would have had available to them, it would not have been two of the three prospective cohort studies. Right?
A. Right.
Q. And they would not have had the follow-up of the

original cohort studies. Right?
A. Yes, and they wouldn't have had other case-control studies.
Q. And one of the things in explaining the finding -- first, the finding was a II-B finding in which chance, bias and confounding could not be ruled out. Do you remember that?
A. Yes. I remember what the title was.
Q. One of the things that the investigators in IARC commented on is a topic that you spoke to us quite a bit about this morning which is the possibility of migration. Do you remember talking to us about that this morning?
A. Yes, I do.
Q. Let's take a look, if we could, on what the scientists at IARC concluded as it relates to migration.

What these folks found is that "perineal exposure to cosmetic talc in women is of concern because of its possible association with ovarian cancer. Several studies have been conducted in women to assess potential retrograde movement of particles through the reproductive tract to the ovaries."

Do you see that?
A. Yes.

Q. Those are some of the studies you spoke to us about this morning. Right?
A. That is correct.
Q. (Reading.)
"These have been conducted in women who were about to undergo gynecological surgery, most of whom had diseases or complications of the reproductive tract and organs that required surgery. The findings reported in these studies may be confounded by the various levels of dysfunction and clearance from the female reproductive tract due to underlying pathologies?"
That's what the IARC scientists said when they did this review?
A. As a gynecologist, I have no understanding of what that means.
Q. My question was: That's what the scientists who did this review concluded in the IARC's published monograph?
A. I don't think there was a gynecologist on this panel. I agree with what you are highlighting.
Q. (Reading.)
"In addition, most of the studies had little or no further information on the use of talc products for perineal hygiene or changes in the habits that may

have preceded surgery."
A. I don't have any reason to understand what that has to do with putting carbon particles or radioactive microspheres in the vagina and seeing them in the pelvis 24 hours later at the time of surgery. Whether or not the person used perineal talc before or after surgery has nothing to do with the conclusion of those studies.
Q. I want to talk to you about the carbon particle study. Let's just finish this paragraph and get right to that.
You know, Dr. Clarke-Pearson, there is a real limitation to have carbon studies in there?
A. Not that I know of.
Q. How many people were enrolled in the carbon particle study?
A. I've forgotten. A small number.
Q. Three.
How many of them were carbon particles found?
A. There were carbon particles identified in the pelvis.
Q. Two?
A. Two out of three.
Q. That study didn't deal with talc. Right?
A. No. It was a particle about the same size as

talc.
Q. And it didn't deal with a particle migrating from the perineum to the ovaries?
A. No, it was in the vagina.
Q. The carbon particle was actually placed inside the vagina near the cervix. Right?
A. Right.
Q. And the women in that study were not standing up. Right?
A. Women stand up; they sit down; they lie down.
Q. Did you look at the study for how the women were positioned in the carbon particle study?
A. They laid suppined for about two hours.
Q. With their head down?
A. I think their hips were up a little bit.
Q. Hips up; head down. Right?
A. Okay.
Q. The women in that study, all three of them were given oxycontin. Right?
A. They were given oxytocin.
Q. Oxytocin. Maybe they would have wanted that.
Oxytocin. Thank you, Doctor.
And the purpose of the oxytocin was to stimulate contractions. Correct?
A. Yes.

Q. And the authors of that study in fact concluded that the oxytocin could have been responsible for the movement of those particles. Right?
A. I would agree. There are other studies that show migration as well.
Q. I want to talk about those, too. Because you said carbon particles, I want to do that one.
Let's talk about what the working group reviewed here. On balance, the working group believed that the evidence for retrograde transport of talc to the ovaries in normal women is weak. Do you see that?
A. I do.
Q. "Normal women." They found that evidence to be weak. Correct?
A. Yes.
Q. "In women with impaired clearance function, some evidence of retrograde transport was found. Studies in animals showed no evidence of retrograde transport of talc to the ovaries."
Is that right?
A. That's right. There was no good animal model to reproduce human anatomy. And getting back to this whole idea of clearance, I don't know what they are talking about.
Q. There is no published study, animal or human,

that actually traces externally applied talc in the perineal region up through the reproductive tract to the ovaries. True?

A. In animal studies?

Q. Or human.

A. I just want to make sure what we are talking about. There has been no experimental study to use talc in this setting of applying it, whether it's on the vulva, perineum, or vagina would be unethical at this point in time.

Q. No study at all, Doctor, that shows that talc applied externally can travel up the reproductive tract to the ovaries. Correct?

A. I think we could go to plausible -- there is no study. You are right.

Q. In fact, there are also no studies in humans that demonstrate the migration of any particulate matter from the external perineum up through the reproductive organs to the ovaries. Right?

A. That's correct.

Q. None of the articles that you cite in support of your opinion regarding migration looked at whether talc can migrate from perineal application through the reproductive organs to the ovaries. Right?

A. That's correct.

Q. Let's look at literally, a bit at a quick chart, if we could, which is slide 27 of the studies that you cite in your report for the proposition that talc can migrate to the ovaries.

We just talked about the Egli Newton 1961 study that showed in two people laying down, given drugs for contractions, that carbon particles that have been deposited up near the cervix were found. Is that right?

A. The carbon particles got to the tubes and ovaries.

Q. This is a real old study. Right, Doctor?

A. 1961. It's a while back.

Q. I don't even have the '60s on my chart. This two-person carbon particle study was available well before you got involved in this litigation. Correct?

A. Yes.

Q. Incidentally, Doctor, I want to make sure we are clear on something. Before Dr. Thompson called you and asked you to look at this literature in connection with this lawsuit, this litigation, you were not of the opinion that talc causes ovarian cancer?

A. That's what we talked about for a good bit this morning already.

Q. I want to make sure we were clear.

So this 1961 studied two people. Then you cite a 1971 study of a radioactive tracer. Right?
A. Right. Of human albumin microspheres that were put in the vagina.
Q. This study was published decades before you got involved in this litigation. Right?
A. Yes.
Q. This study had a total of 21 people and found that this radioactive tracer traveled in nine of them. Right?
A. It got to the tubes and ovaries 24 hours roughly after it was applied in the vagina.
Q. In less than half these folks. Right?
A. Yes.
Q. Do you remember whether these folks were standing up?
A. If a woman is going to surgery the next day, she probably slept in bed the night before, supine or prone, depending on how she chooses to sleep, and was probably standing up to come into the operating room. I think she was in a variety of positions. Had to be.
Q. When the radioactive tracer was placed inside the vagina, she was not standing up?
THE COURT: The answer didn't come out on the screen. The last question was: When the radioactive

tracer was placed in the vagina, she was not standing up. Now, I need your answer.

THE WITNESS: I'm sure at some point in time, the 24 hours before surgery, she was standing up and lying down, and probably sitting.

Q. The question was really simple. When they conducted this study and they placed the radioactive tracers up near the cervix, these women were lying down?

A. Yes, that's what I said. Also, they were probably in a lithotomy position, as you do a routine pelvic examination.

Q. The only other study you cite in the body of your report that deals with particles being placed inside a woman and later followed is this 2004 study you see up here?

A. Yes.

Q. That one had to do with an examination done by a doctor wearing cornstarch-dusted gloves. Correct?

A. Yes.

Q. And these gloves were also placed inside of the women. Correct?

A. In the vagina.

Q. And in this study there were 27 people involved. Correct?

A. Yes.
Q. And so in terms -- and this final study that you cite doesn't involve people. It's actually a chapter in a 2006 textbook. Right?
A. I believe so.
Q. And there is one sentence in there about dead sperm being transported by uterine contractions. Right?
A. I talked about that this morning.
Q. In terms of the total number of people who had a particle inserted inside of them, and then they were followed to see what happened to the particle -- we are talking about 38 people. Fair?
A. These are experiments. Yes, 38 people, if that's your count.
Q. That's just the thing. These are experiments. Right?
A. Yes, and they demonstrate migration of talc -- migration of particles from the vagina to the tubes and ovaries within 24 hours.
Q. And can we take a look at the graphic of the positions that were described in these articles of how the women were when these particles were inserted. This is consistent with your review of these studies in terms of women lying on their back with their heads

15 degrees down to the ground. Right?
A. Yes. I would have to look at the studies to see how long they were held in this position.
They weren't held in this position for the next 24 hours while they were waiting to undergo surgery.
Q. In further support of your opinion that an external application of talc can in fact migrate to the ovaries, you cite a number of studies that looked at the tissue of women, right? The Heller and the Henderson studies?
A. The ovarian tissue found at the time of surgery.
Q. And if we could look at that slide, please.
None of the tissue studies that you cited did a connection between the alleged exposure to talc and the number of particles that were found. Correct?
A. I'm not quite sure I understand your question.
Q. In the Heller study, for example, they were unable to show a connection between how many particles were found and how much talc a person claimed to have used. Right?
A. I guess the point that I thought you were trying to make is that the talc got to the ovaries somehow.
Q. In the Heller study, the authors note that they were unable to make a connection between reported use

of talc and a finding of talc in the ovaries. Right?
A. So some of the patients in that study had used talc and others hadn't, and he found talc in both groups of patients. Is that what you are talking about?
Q. In part, Doctor. 24 people in the study. Right?
A. And some people reported many years of talc use, correct.
Q. There was not a correlation between increased reported use of talc and an increased number of particles found in the ovaries. Right?
A. But it showed talc particles in the ovaries.
Q. One of the things about that study, though, Doctor, is that they looked at the pathology of one of those particles and reported it. Right?
A. I believe so, yes.
Q. And there was no inflammation noted. Right?
A. I think the point is the talc can get to the ovary from the vulva if the patients were dusting themselves, or they may have gotten talc exposure when they were babies.
Q. They found talc in the tissues of people who didn't report ever using talc -- they found talc in the tissue of women who never reported using it for

female hygiene. Right?
A. Female hygiene, but they may have been exposed as infants.
Q. When they looked at a pathology slide to see if that particle of talc or the particles of talc had any inflammation, they didn't find it. Right?
A. You are talking about one slide?
Q. I'm talking about the reported paper.
A. You just mentioned one ovary they found talc in?
Q. The paper, you know, Doctor, because you reviewed it, it reports on a review of one of the slides. Right?
A. Right.
Q. And there was no inflammation found associated with the talc that they found.
A. I don't think I have been sitting here all day saying that one talc powder causes inflammation that's going to cause cancer. It could, but it doesn't necessarily occur in every single patient.
Q. Let's get that straight. I thought we just went through the fact that you do not believe there is a threshold of exposure to talc below which ovarian cancer does not develop?
A. We don't know that threshold, but not every talc particle necessarily causes chronic inflammation. So

they may not have seen it on that one microscope slide of talc in that one ovary.

Q. So it's your testimony, Doctor, that some talc reaches the ovary and some talc causes chronic inflammation. Is that right?

A. Yes, in some patients.

Q. And you have not attempted to quantify how much talc that reaches the ovary produces a chronic inflammatory response. Correct?

A. No. It may not have to do with the volume of talc. It may have other things to do with the particular woman.

Q. And there are zero studies that you could point the Court to that would support your position that some but not all of the talc particles that get to the ovary produce a chronic inflammatory response?

A. I believe, and there is evidence that talc causes a chronic inflammatory response. It may not be in every patient. Not every person that smokes cigarettes three packs a day for 20 years develops lung cancer. Some patients may be more susceptible to the talc than others.

Q. And as it relates to what determines whether or not a particle of talc causes chronic inflammation or does not, you are not aware of any scientific

literature that would support that opinion. Correct?
A. That's true.
Q. Your report and your presentation --
MS. BROWN: Your Honor, did you want to follow up on that?
THE COURT: Are you finished with this?
MS. BROWN: I was going to move to inhalation briefly.
Q. Your report and your testimony this morning suggests that you think that inhalation is a possible route of exposure?
A. I do.
Q. That's not what you told us in your deposition, though. Right, Doctor?
A. I would have to see the deposition again.
Q. It is true, is it not, Dr. Clarke-Pearson, that you haven't seen --
MS. BROWN: Well, go ultimately to 219.
THE COURT: I thought you were reading from the deposition.
MS. BROWN: I'll eventually do that. 219, 14 to 23.
Q. You were asked about inhalation as a potential route of exposure in your deposition. Right, Doctor?
A. Yes.

Q. And your testimony was that to date we haven't seen an increased risk of ovarian cancer with inhaled talcum powder. Right?
A. Yes.
Q. And what you testified to is that the -- if inhalation was in fact a viable pathway for talc exposure to the ovaries, then you would expect in the epidemiology to see an increased risk with nongenital use of talc. Right?
A. And the Schildkraut study does show that.
Q. What you testified to in your deposition is that we don't see that. Right?
A. That's what I said in my deposition. I think I reread lots of these papers again, and the non-genital use of talc, the talc in the Schildkraut study shows an increased risk of ovarian cancer.
Q. You haven't attempted to compare a number of nonstatistically significant findings of nongenital use of baby powder with the Schildkraut finding; did you?
A. No. I just think the Schildkraut findings are data we should consider, and they raise the plausibility of transport from inhalation.
Q. You think transport from inhalation is very unlikely. Correct?

A. I think I said that earlier.
Q. In fact, you think your primary opinion is related to the migration theory. Correct?
A. Yes.
Q. You testified in your deposition, in fact, that powdering someone's baby with talcum powder does not increase the mother's risk of ovarian cancer. Right?
A. If I said that in the deposition; I would say, yes, that's true.
Q. Well, is that your opinion?
A. Yes.
Q. I heard you testify with counsel this morning that you considered the totality of the evidence. Right?
A. Yes. That's what I tried to do.
Q. But that is what you testified in your deposition. Correct?
A. I don't recall testifying to that in my deposition.
Q. You did not mention in the body of your expert report any of the cohort studies. Correct?
A. That's true.
Q. You did not list on the reliance list for your paper your main cites, you did not include a cite to any of the cohort studies. Correct?

A. I'm not sure of that.
Q. We can look at it. What you told us in your deposition is that you don't think the cohort studies contribute to your review one way or another. Right?
A. So as individual cohort studies or as a body of evidence based purely on the cohort studies, I can't consider them useful in terms of going to the totality, and that's what we're trying to talk about. What I did was to look at the case-control studies, the cohort studies, and the pooled studies, and then the meta-analysis. So looking at the totality, the meta-analyses, were much more helpful and stronger evidence to identify the real outcome of use of talc in the perineal area which increases the risk of ovarian cancer in every one of those meta-analyses.
Q. Let's focus on the question, which was that you don't believe the cohort studies contribute one way or another to your review of the literature here?
A. They contribute to the meta-analysis, yes.
MS. BROWN: Your Honor, permission to read?
THE COURT: Yes.
Q. Let's look at your deposition, page 145, lines 7 to 17. You were asked:
"QUESTION: How can you validate completely excluding cohort studies from your discussion?"

There was an objection.

"ANSWER: Because I don't think they contribute one way or the other. They are poorly designed, poorly executed, and the data that they provide does not inform us at all. In fact, these meta-analyses in many cases include the cohort studies and still came out with a statistically significant increased risk of ovarian cancer."

That was your testimony. Right?

A. Right. And the cohort studies were included in the meta-analysis, so I was considering them in that setting, but just not isolated as cohort studies.

Q. You don't think the cohort studies contribute one way or the other?

A. They contributed to the meta-analysis; and even though they were not very strong studies in many ways, and were not statistically significant, they did show an increased relative risk. They were included in the meta-analysis, and they didn't bring down the fact the meta-analysis showed a statistically significant increased risk of developing ovarian cancer with perineal task use. If I excluded them, the results in the meta-analysis would have been even more negative in the use of talc in the perineal area.

Q. You know the Penninkilampi meta-analysis did not

include the Gates follow-up in 2010?
A. Right. He chose to use another of the Nurses' Health study.
Q. Two were not true. You testified at your deposition that you don't think the cohorts contribute one way or another?
A. As cohort studies just by themselves.
Q. I want to talk briefly about some of the meta-analyses that you did include in your chart here and talk about whether what the authors say fits what you are using these studies for here in court. Okay?
A. Okay.
Q. Let's start, if we could, Doctor, with the Huncharek 2003 study which was available at A-67 in your binder at A-67. This is a 2003 meta-analysis.
Before we leave this table, five of the six meta-analyses that you list on this table were available at the time you went on Fox News in 2014 to talk about ovarian cancer. Correct?
A. Yes. I wasn't necessarily aware of all them. They are not in the GYN literature.
Q. Five of the six studies were published and publicly available peer-reviewed scientific literature at the time you went on Fox News in 2014. Correct?
A. That's correct, but I don't read the thousands

of papers published in the publically-available literature every day.

Q. What you do is you rely in part on leading public health and professional organizations to review and summarize the literature that you don't get to yourself. Right?

A. That's one source of my information for medical decision-making.

Q. And none of those organizations, public health or gynecologic communities, have concluded what you concluded here that talc causes ovarian cancer?

A. Correct.

Q. Let's take a look at this article at A-67, one of the six meta-analyses that you cite from 2007. Let's look at what the authors of this study conclude, which is that:

"The available observational data do not support the existence of a causal relationship between perineal talc exposure and an increased risk of epithelial ovarian cancer. Selection bias and uncontrolled confounding may account for the positive association seen in prior epidemiological studies."

Do you see that, Doctor?

A. Yes, I see that.

Q. Huncharek 2003 explicitly states that the

existence of a causal relationship is not supported by the data. Correct?

A. That's what they say in their narrative. If you look at their statistics, the risk is statistically increased.

Q. They are not talking about statistically significant associations. They are talking about whether the data supports a causal relationship. Right?

A. So this is a significant risk factor that they have identified as have all the meta-analysis that you have there on my table plus Berge, and those all increased the risk of ovarian cancer and I believe are causative of ovarian cancer. If you do a Bradford Hill analysis, the causation fits.

Q. What the authors of this paper say is that:

"Overall, the above findings of selection bias due to study design and the clear lack of a dose-response relationship between talc use and ovarian cancer brings the previously suggested association into question. The data presented in this meta-analysis do not support a cause effect relationship between perineal cosmetic talc use and the risk of ovarian cancer development?"

Do you see that?

A. Yes, I do.
Q. You cited this study in your paper in support of your opinion that talc causes ovarian cancer. Right?
A. And this paper, I think it's your top one on the chart -- it's the third one from 2003, it's a 33 percent increased risk of ovarian cancer occurring in talc use.
Q. You cite this paper in support of your opinion that talc causes ovarian cancer. Correct?
A. That's correct.
Q. The paper itself states that the data do not support a causal relationship. True?
A. That's what the authors say.
Q. Let's take a look at another one you cite, Gross and Berg, from 1995. And that, Doctor, can be found at 509 in your binder.
You also cite Gross and Berg in support of your opinion that talc causes ovarian cancer. Correct?
A. Yes.
Q. The Gross and Berg authors do not state that. Fair?
A. Oh-oh, what exhibit is, this --
MS. BROWN: 509.
MS. O'DELL: A-509?

MS. BROWN: Clarke-Pearson 509.

Q. Let's look at what the authors of this meta-analysis from 1995, and just to get our bearings here, Doctor, this is way back in the 1990s. Right?

A. This one, I don't see it on the paper here today. This paper was done before the one you just talked about. So it includes less case-control studies and cohort studies. So we're sort of going backwards in time, the way you are doing this.

Q. So what we are doing is we are looking at the studies that you cited in support of your opinion in this court that talc causes ovarian cancer, and what we're looking to see is if the authors who wrote them and published them in a peer-reviewed literature said the same thing.

A. Okay.

Q. Let's look at Gross and Berg and see what these folks say, quote:

The purpose of this paper is to examine, "talks about the concern of talc and ovarian cancer" -- "the purpose of this paper is to examine whether this concern, heightened by several epidemiological studies purporting to show an increased risk is valid. The conclusion reached herein is that the evidence regarding the risk of ovarian cancer associated with

talc exposure is equivocal, and further examination of the relationship is required before a sound conclusion can be made."

Do you see that?

A. Yes.

Q. The authors of this study did not conclude that talc causes ovarian cancer. Right?

A. That's what they are saying, yes.

Q. And, in fact, this meta-analysis is particularly helpful as you will recall from reviewing it in highlighting some concerns about meta-analyses in general. Right?

A. I forgot if they made some commentary about that.

Q. Let's look at what the authors who conducted this meta-analysis said.

First of all, let's take a look at the studies that they combined, and you will agree with me, Doctor, if we just look at the relative risk and the odds ratios we can see that only one of these studies reaches statistically significant. Right?

A. Of these six studies -- this goes way back in time. There are many, many studies since then. If you look at the relative risk in the table, you are showing me most are elevated. 61 percent, 40 percent,

10 percent.
Q. This is one of the six meta-analyses that you chose to include in your litigation report supporting your opinion that talc causes ovarian cancer. Correct?
A. I wanted to submit the totality of the evidence that is there in the medical literature, so, yes, it is included in my report.
Q. And you forgot the most recent, Berge 2018 analysis?
A. It was a total oversight on my part. I admit the errors. That wouldn't have changed the outcome of my conclusions or the other meta-analyses.
Q. Well, look at what their conclusions were. To make it easy, you can just agree with me, those authors say you can't establish a causal relationship on this data.
A. This data doesn't include a full blown evaluation of Bradford Hill, which is the causation that we have been talking about.
Q. The Berge authors from 2018 conclude that you cannot make a causal relationship between talc and ovarian cancer?
A. No, they didn't do a Bradford Hill then.
Q. You say it was an oversight that it wasn't

included, but that it would not have changed your opinion at all. Right?

A. Right.

Q. We can agree, though, the authors of Berge do not state that talc causes ovarian cancer?

A. We can agree to that.

Q. Let's go back to the Gross and Berg where they identify some of the issues with the meta-analysis.

"If, for example, the issue of study bias has not been properly addressed, spurious associations due to small biases may reach statistical significance when the studies are combined because the sample size in effect has increased."

Do you see that?

A. I see that.

Q. They include a quote:

"In any one study the bias may fail to be great enough to give rise to statistically significant. But with meta-analyses, such biases can combine so as to give rise to an overall appearance of statistical significance."

That was a concern that these authors of this meta-analysis raised in the article you cite. Correct?

A. Yes.

Q. These authors also commented about limited evidence supporting a dose or duration response relationship. Right?

A. Based on the small number of cohort studies in 1995, yes.

Q. This is the 1995 meta-analysis you put in your report to support your opinion. Right?

A. Yes, along with all the other meta-analyses and the totality of the epidemiologic data.

Q. And what these authors state is that

"Given the rather low relative risks reported in the studies along with the existing biases and confounders that have not been adjusted for, a claim for an increased risk should be viewed with some suspicion?"

Correct?

A. That's what they say.

Q. The authors of the Gross and Berg 1995 meta-analysis did not conclude that talc causes ovarian cancer. Right?

A. Right.

Q. Let's take a look at one more, Doctor. We're almost done.

I want to talk to you about another meta-analysis that you included which is the Langseth.

You can find that at A 88. And to orient us, this is another meta-analysis that you put on your chart here in support of your opinion that talc causes ovarian cancer.

We can agree -- and we'll take a look, but we can certainly agree that the authors of that study do not agree with you. Correct?

MS. O'DELL: What exhibit number for Langseth?

MS. BROWN: A 88.

A. You will have to show me.

Q. This is the Langseth article, Exhibit A 88, that you cited in your report, perineal use of talc and risk of ovarian cancer. Right?

A. Yes.

Q. And what the authors of this study include in their published peer-reviewed publication is a proposal to the research community. Right? Do you see that?

A. Yes.

Q. What the authors, having conducted this study, state is that, quote:

"The current body of experimental and epidemiological evidence is insufficient to establish a causal association between perineal use of talc and ovarian cancer," quote.

Do you see that?
A. I do.
Q. The authors of this study did not conclude, as you have done here, that talc causes ovarian cancer. Right?
A. That's what they say.
Q. And, in fact, one of the things they did was include this forest plot of some of the studies, the cohort studies that they combined in this meta-analysis. Right?
A. Those are the studies they used in their meta-analysis, and nearly all the relative risks are above 1.
Q. And you were asked some questions about this forest plot in your deposition, and you know that only 10 of the 20 studies included here reached statistical significance. Correct?
A. Subsequently, there have been other studies, and the majority today and the most recent meta-analysis show the majority are statistically significant. So you are picking a point in time before most recent data is in.
Q. The truth of the matter, Dr. Clarke-Pearson, is that the medical community as a whole does not agree with the opinions that you have given to this Court

today. Right?
A. I don't know if they agree or disagree. They haven't taken a stand on this.
Q. The gynecologic oncologist medical community has not reached a consensus that talcum powder causes ovarian cancer. True?
A. I think there is a variety of opinions in that community.
MS. BROWN: Permission to read, Judge?
THE COURT: Yes.
Q. Let's take a look at your deposition, page 25, lines 20 to 23. Your February 4th, 2019, deposition you were asked:
"QUESTION: Has the gynecologic oncologist medical community reached a consensus that talcum powder causes ovarian cancer?
"ANSWER: As best I know, not at this time." Right?
A. That's correct.
Q. The gynecologic medical community has not reached a consensus on the opinions that you have given to this Court today. Correct?
A. That's right.
MS. BROWN: Your Honor, I have no further questions at this time.

THE COURT: We'll take a break for a few moments.

THE DEPUTY CLERK: All rise.

(Recess.)

(Continued on the next page.)

///

THE DEPUTY CLERK: All rise.

THE COURT: Thank you.

DANIEL CLARKE-PEARSON, resumed.

THE COURT: I want to ask a couple of questions of the witness.

Just to follow up on a couple of the items that you testified, Dr. Clark-Pearson, first on some of the questioning at the end of the questioning on inflammation, and when you indicated not every talc particle is going to cause inflammation. Correct?

THE WITNESS: Yes.

THE COURT: Your answer in that regard was in trying to explain that it depends on the woman.

THE WITNESS: That's part of it. The immune system of that woman, where that talc particle lies, those are the variables.

THE COURT: Those are the basic variables as to why it makes a difference?

THE WITNESS: I think so. And I think the tissues' susceptibility of the ovary may vary a little bit from one woman to another. We're not saying talc is causing cancer in the vagina or cervix or uterus. The ovary itself, I believe, is susceptible for

reasons that are not clear.

THE COURT: You said "for reasons that are not clear"?

THE WITNESS: Yes. That I think likewise we don't know exactly why smoking causes lung cancer. There's chemicals there, but exactly what it causes and why some people smoke and don't get cancer and others do, the immune system is probably a big part of it, the genetics of the patient.

THE COURT: The last question, and I asked you this this morning, following on the inhalation theory. Just to press you a little bit more on that, which is I think you have been very candid to say you've used the words "very unlikely that it will happen."

THE WITNESS: Okay.

THE COURT: But, nonetheless, you continued to assert that it's plausible that it can.

THE WITNESS: There is evidence -- I guess I'm extrapolating from asbestos particles itself and those talcum powder has asbestos in it or not --

THE COURT: That's something that's an open question in this case.

THE WITNESS: Yes.

THE COURT: If you were to take the asbestos out of it, would you still have the same opinion on

inhalation?

THE WITNESS: Probably less so.

THE COURT: So there is a difference in your opinion if it were found not to have asbestos?

THE WITNESS: Yes.

THE COURT: You think it's the asbestos quality of it as one of the components that makes the inhalation theory more plausible?

THE WITNESS: Yes.

THE COURT: Even if still very unlikely?

THE WITNESS: And, again, based on IARC findings that inhaled asbestos can get into the ovary.

THE COURT: I think I have where you are on that. But I'll still end by saying, I don't think that's where the bulk of your opinion lies.

THE WITNESS: No. You are correct. Thank you.

THE COURT: Thank you, Ms. O'Dell. None of that counted toward you.

MS. O'DELL: May I expand on the question that your Honor asked?

REDIRECT EXAMINATION

BY MS. O'DELL:

Q. Dr. Clarke-Pearson, you mentioned asbestos

fibers in relation to inhalation and that impacts your opinion. Would that also be true for talc fibers or fibrous talc?

A. Sure. If I didn't say it just now, yes, I'll answer your question by saying fibrous talc would be the equivalent of impact, as talc has asbestos fibers.

Q. Thank you.

At the end of Ms. Brown's questioning she was asking you about consensus in the medical community, and then she asked you questions about consensus in the GYN oncology community. Do you recall those questions?

A. Yes, I do.

Q. Can there be differences of opinion in the medical community?

A. There are always differences of opinion where there is clinical decision-making or policy. So, yes, I think there are differences of opinion. I think right now the medical community is silent on the topic. I'm not sure there is a difference of opinion.

Q. In regard to your opinion based on your review of the evidence, the totality of the evidence, is it your opinion that there is -- it is biologically plausible that talc can reach the ovary?

A. Can reach the ovary, that's the first question,

yes.
Q. Based on your review of the evidence, is it your opinion that talc, once it reaches the ovary or the Fallopian tube, causes chronic inflammation?
A. Yes.
THE COURT: What can cause chronic inflammation? Based on your previous testimony, it's not going to cause it in every case.
THE WITNESS: Right. All the things I had on that one graphic -- endometriosis, chronic pelvic inflammatory disease, obesity.
Q. Based on those two facts, is it your opinion in this case, having considered the totality of the evidence, that it is biologically plausible that the genital use of talc can cause epithelial ovarian cancer?
A. Yes.
Q. I'm going to change topics.
Doctor Clarke-Pearson, I'm going to skip around to try to address a few things.
You were asked a number of questions about whether you considered the cohort studies in reaching your opinion. You gave testimony about that earlier?
A. Yes.
Q. You recall that?

A. Yes.
Q. Did you read the cohort studies prior to reaching your opinions in this case?
A. Yes. I just didn't acknowledge them maybe the way people wanted me to in my report.
Q. And, in fact, are the cohort studies part of the reliance materials that you included at the back of your report?
A. Yes. And that was part of the totality of my assessment.
Q. And, also, in regard to the Berge study, you were very forthright to say it was an omission not to include it in the chart of meta-analyses, and you've talked about that.
A. Right.
Q. Did you consider the Berge study prior to reaching your opinions in this case?
A. I did. I just didn't happen to have it on my table in my report.
Q. In fact, did you include the Berge study in your reliance materials that were included in the back of your report?
A. I believe so, if you look at that reference list.
Q. I will.

Dr. Clarke-Pearson, did you include Berge in your reliance material?

A. Yes, it's right there on the reference list.

Q. I think Ms. Brown was alluding to the cited references and suggested that you had not included it in your report, but in fact you had. Correct?

A. I see, yes.

Q. There were also questions regarding the 2010 IARC monograph, the talc monograph pertaining to talc without asbestiform fibers.

A. Yes.

Q. You were asked a series of questions regarding their findings in that particular monograph. Let me ask you a couple of questions.

In IARC 2010, did they consider the data after 2006?

A. In their references, the citations that they had, go up to I think just to 2006. There is a four-year gap of information that was coming out into the medical literature that were not considered.

Q. In fact, if you looked at the charts we looked at earlier, the forest plots that were part of our original presentation, would it be fair to say that all of the case-control studies after Wu, Rosenblatt, Kurta, Wu, 2015, Cramer and Schildkraut were not a

part of IARC's consideration for the 2010 monograph?
A. Right. They couldn't have known that because it was after they published.
Q. And also, in regard to the IARC 2010 monograph, did they consider the meta-analyses that you've discussed here today that were published after 2006, and that would include Langseth 2008, Berge 2018, Taher 2018, not published -- excuse me I skipped Penninkilampi -- Penninkilampi 2018 and Taher 2018, and then also Terry 2013, were those a part of IARC 2010 analysis?
A. They couldn't have been because they were published subsequent to that which adds, again, to the totality of what I have been trying to talk about today.
Q. Before lunch Ms. Brown asked you about a reference, a publication that you wrote for the New England Journal of Medicine relating to screening for ovarian cancer. Do you recall those questions?
A. I do, yes.
Q. She directed your attention -- by the way, was this an invited review of the New England Journal of Medicine?
A. Yes. I was asked as an expert to write a review paper, so it took a fair amount of time to review the

world's literature on this topic.
Q. Did you consider that to be an honor?
A. Yes.
Q. Looking at the section Ms. Brown directed you to that addressed risk factors, it says:
"Risk factors other than age, a family history of ovarian cancer, breast cancer, and the presence of BRCA mutation are poorly understood and approximately 90 percent of ovarian cancers appear to be sporadic."
Did you include in that recitation of risk factors any inflammatory risk factors that we discussed this morning?
A. No. The risk factors I listed are the ones that are high risk like BRCA mutations.
Q. Would those be considered genetic risk factors?
A. Yes.
Q. And for that reason, because they were genetic risk factors as opposed to inflammatory risk factors, would it have been appropriate to list other risk factors such as talc usage?
A. The paper was intended to identify patients to discuss whether screening was possible at all, and the answer was no; and it still is no on the one hand, discouraging physicians from doing testing, such as ultrasounds or CA-125 blood tests, which at that point

were proven to be not useful but they were still being done and to encourage the medical community to do more research to identify screening techniques, and we still haven't gotten there in the 10 years since I published that paper. It wasn't intended to review all risk factors.

Q. Dr. Clarke-Pearson, you were asked about the NCI publication, "Ovarian Fallopian Tube and Primary Peritoneal Cancer Prevention," the PDQ as it's referred to. Do you recall the line of questions Ms. Brown asked about?

A. I do remember some. Some of my comments were the references were pretty far out of date.

Q. Let's turn and look at the five references that are related to ovarian cancer and talcum powder usage.

You see 43 through 47, Huncharek 2003. Is that one of the meta-analyses that you included in the chart that we looked at earlier?

A. Yes, it was one of the older ones.

Q. Did it include there was an increased risk in the use of talcum powder for that ovarian cancer?

A. The answer is yes, about a 33 percent increased risk that was statistically significant.

Q. And also for the PDQ, they cite the Terry paper. Do you recall that?

A. The pooled analysis.
Q. And in the Terry paper did they include that there was a 1.24 increased risk of ovarian cancer that was statistically significant?
A. Yes. It's highlighted there.
Q. And, further, while I'm on the Terry paper, let me follow-up on another item Ms. Brown asked you about, and, specifically, on whether the Terry paper showed a trend toward dose-response. Do you recall those questions?
A. I recall that, and it does show a trend.
Q. In fact, does the paper include a table that outlines the statistically significant results of the increased risk for certain quartiles of usage?
A. Yes.
Q. Is this the table that shows that there was a statistically significant trend in dose for the Terry study?
A. Yes.
Q. And go further, so we've discussed Huncharek cited by the NCI that showed an increased risk. We've discussed Terry cited by NCI, which also showed or demonstrated an increased risk. And then they go to Schildkraut. And in the Schildkraut paper, of course, you and I discussed that this morning, was there a

statistically significant increased risk for ovarian cancer?

A. Yes. In the specific population of African-American women from, I think, 11 different areas of the United States.

Q. In the Schildkraut paper -- and could we put it up on the screen? It's Exhibit 8. It's General Causation Opposition Exhibit 8. If you could go to page 1416 of the publication, which I think is the next to the last page.

On the left side, the lower paragraph there, Doctor, did the researchers in the Schildkraut study write:

"The results of the current study showed that genital powder use was associated with ovarian cancer risk in African-American women and are consistent with localized chronic inflammation in the ovary due to particulates that travel through a direct transvaginal route. The dose-response observed for duration of genital powder use provides further evidence for the relationship between genital powder and overall EOC risk. Our data suggests that the increased risk due to the use of genital powder applies to both serous and non-serous histologic subtypes."

Is that what they concluded?

A. Yes, that was their conclusion.
Q. Is that consistent with your opinion?
A. Yes. In the paper and the totality as well.
Q. Going back to the PDQ, we talked about Huncharek, Terry, Schildkraut, Gertig.

Dr. Clarke-Pearson, did the Gertig study, one of the cohort studies show a statistically significant increased risk in serous ovarian cancer?
A. In serous ovarian cancer, which is the most common histologic type of the epithelial ovarian cancers, yes, they did.
Q. Based on the fact NCI cited five references, and the four we have gone through show a statistically significant increased risk, is it somewhat baffling to understand how the NCI concluded there was no data to support a relationship between the genital use of talcum powder and ovarian cancer?
A. It's baffling, and, at the time this is a very recent publication. There is so much other literature equivalent to those four articles you just presented to me that exist that could have been analyzed. I'm disappointed the NCI isn't doing a better job of doing good comprehensive research.
Q. You were asked some questions -- I'm going to transition to another topic. You were asked questions

about some of the studies that you relied on in connection with your opinion that talcum powder can migrate to the fallopian tubes and ovaries. And, in particular, counsel for Johnson & Johnson stated in relation to the Venter paper, that the Venter paper does not support your opinion that talc can migrate. Do you recall that line of questioning?

A. I've forgotten it.

Q. That's fair enough. You've had a long afternoon.

Take a look at the Venter paper, which is general causation opposition 70.

The Venter paper discusses the migration of radioactive tracers?

A. Right. Albumin microspheres that are radioactive.

Q. And in the discussion section of the paper, let's look at the conclusion that the authors reached there.

Based on their study, this experiment, they stated:

"Evidence is available for migration of different substances in either direction within the female reproductive system between the peritoneal cavity and ovaries via the tubes, uterus, and the

vagina, and out."

Is that supportive of your opinion that the female reproductive system is an open system?

A. Yes, it goes both ways.

Q. They go on to say:

"Various living organisms actively follow this pathway in both directions. Gases, fluids, bias and contrast media can easily be introduced from the vagina into the peritoneal cavity. If the transit can take place so easily, it is probably the same for many chemical substances used for hygienic, cosmetic, or medicinal purposes, many of which may have potential carcinogenic or irritating properties."

Is that also true of talcum powder?

A. Yes.

Q. You were asked a series of questions about one of the Huncharek papers, and this in particular was the Huncharek 2003. There are three of the Huncharek papers, but this is 2003, and it was marked by Ms. Brown as A 76. Do you recall that? Ms. Brown directed you to the material I have highlighted in pink.

Ms. Brown highlighted, walked you through what I have highlighted in pink:

"The available observational data do not

support the existence of a causal relationship between perineal talc exposure and an increased risk of epithelial ovarian cancer."

I'm sure she was pressed for time. She missed a paragraph here. It goes on to say:

"These statistical associations raise concerns that there may be a cause effect relationship between perineal talc exposure and ovarian cancer carcinogenesis. This is further confirmed by the structural similarities between talc and asbestos, a well-recognized human carcinogen."

Did the authors state that?

A. Yes, they did.

Q. Let's go to one more of the studies that Ms. Brown directed you to. It was the Gross and Berg study. Do you recall that?

A. Yes.

Q. That was one of the early meta-analyses that you reviewed?

A. Yes.

Q. Dr. Clarke-Pearson, why is it important when you are looking at meta-analyses to review and rely on the most recent meta-analyses?

A. Well, I think we want to look at all of the data, and that particular paper was early on, and

there were very few studies that had been completed at that time. So there is nothing wrong with that meta-analysis, but there are more up-to-date meta-analysis that are much stronger in helping us come to a conclusion about risks.

Q. Did the most recent meta-analyses due to the fact that they analyze, I think you said, 27 studies this morning, do they have greater statistical power?

A. Yes, they do.

Q. And because of that, would they provide further information regarding the true risk between genital talc use and ovarian cancer?

A. Yes, they are the most up-to-date information we could base decisions on.

Q. Let me ask you to look at the Shan and Liu -- it's General Causation Opposition Exhibit 109. If we could put that on the screen.

Ms. Brown discussed with you the first page of this paper, on the right-hand side at the top, and right under "Etiology of EOC Inflammatory in Nature." Do you see that section?

A. Yes.

Q. Just for those of us who don't operate in the medical community all the time, what does "etiology" mean?

A. The reason that some event happens, I guess, if I can put it in a generic term, why something happens.

Q. Ms. Brown directed you to the first sentence:

"EOC is perhaps one of the most sinuous human cancers. In an effort to identify the causes of EOC, a few hypotheses have been put forward" and she suggested that inflammation was a hypothesis. Do you recall that?

A. The incessant ovulation, we're talking hypotheses and inflammation being one, she was suggesting.

MS. O'DELL: And, Cory, if you could put it on the screen, I think it's page 3108 of the article, the second page of the publication.

Q. On the right-hand side, second paragraph at the beginning. The authors write:

"Because inflammation is known to be a causal factor in promoting tubal tumorogenesis the hypothesis that a portion of serous ovarian carcinomas may originate in the fallopian tube provides another link although indirect between inflammation and EOC."

Does that support your opinion, Dr. Clarke-Pearson, and is this one of the reasons you cited this particular paper?

A. That, and it ties in with earlier this morning

talking about the fallopian tube making a contribution to cause serous ovarian cancer.

Q. Let me direct you now, Dr. Clarke-Pearson, to the Penninkilampi paper. We discussed that quite a bit today.

A. Yes.

Q. If you'll turn to page 2 of the publication, and, for the record, it is General Causation Exhibit 62. It's page 42 of the publication.

Ms. Brown directed you to the upper left column at the top, end of the paragraph, and she read:

"The association between perineal talc use and ovarian cancer is based on the body of knowledge from observational study, and most of these have been retrospective case-control studies prone to recall bias. Hence, while perineal talc use has not been shown to be safe, in a similar regard a certain causal link between talc use and ovarian cancer has not yet been established."

Do you recall her reading that to you?

A. Yes.

Q. It's reference 8 and 9, and reference 8 is Huncharek 2011. And just for ease, let me just put Huncharek 2011 on the ELMO. It's General Causation Opposition Exhibit 155.

Is this one of the meta-analyses you reviewed in reaching your opinions in this case?

A. Yes.

Q. And looking at the results of the meta-analyses, did they conclude:

"These reports show roughly a 30 to 60 percent increased risk of ovarian cancer associated with perineal talc exposure."

A. That's what I have been saying all day, yes.

Q. And, in fact, on page 5 of the publication Huncharek 2011 -- it's page 5 on the copy I have.

MS. BROWN: I don't think Huncharek 2011 is one he relied on.

MS. O'DELL: It's on his reliance list.

Q. Let me put it on the ELMO. Huncharek 2011 was another publication by Huncharek and others, and you see it says here:

"Asbestos fibers in the lung initiate an inflammatory and scarring process, and it has been proposed that talc as a foreign body might initiate an inflammatory response."

There is one other section let me just go to quickly.

MS. BROWN: What's the exhibit number?

MS. O'DELL: 155.

Q. Doctor, I think I picked up the wrong Huncharek. I think there are three of them. I'll come back to that.

Back to Penninkilampi. Penninkilampi cited for purposes of the conclusion that -- or, the statement that Ms. Brown directed you to, it says --

MS. O'DELL: I may need a technical assistant on this.

(Pause.)

Q. Ms. Brown took you to this statement regarding a certain causal link between talc use and ovarian cancer has not yet been established, and we looked at Huncharek, and it did show a statistically significant increased risk. And it also cites Langseth, and Ms. Brown asked you about the Langseth paper, and she directed you to certain portions, but let's go back and take a look at other portions.

On page 1 of the Langseth study, Dr. Clarke-Pearson, it says:

"From pathology studies it is known that particles and fibers can enter the body and migrate to distant organs. For instance, asbestos fibers have been found in ovaries for women exposed to asbestos. Analogously following the perineal application talc particulates can migrate from the vagina to the

peritoneal cavity in the ovaries."

Does that support your opinion regarding migration?

A. Yes, it does.

Q. Further in the Langseth study I think Ms. Brown focused your attention on this portion that talked about proposal:

"The current body of experimental and epidemiological evidence is insufficient to establish a causal association between perineal use of talc and ovarian cancer. Experimental research is needed."

They focused your attention on that portion of the study. Correct?

A. Correct.

Q. If you turn over to the back, I think you had time to go to this, it says, quote:

"The mechanism of carcinogenicity may be related to inflammation. This paper focuses on the high degree of consistency in the studies accomplished so far, and what should be the focus in future studies."

Does that also support your opinion that it is biologically plausible that talcum powder can reach the ovary and cause chronic inflammation?

A. Yes, both events are plausible and necessary to

support the causation of talc causing ovarian cancer.

Q. Two more topics.

The CDC has this as part of their website. Ms. Brown showed you this earlier. She put it on the screen with a slide, but in our books we got a printout from the website. It lists risk factors for ovarian cancer, and you walked through those earlier. Right?

A. Yes.

Q. And has the CDC sponsored a systematic analysis of the literature regarding ovarian cancer and specifically sort of evolving paradigms and research in ovarian cancer?

A. Yes. I'm aware of that recent monograph and the group that put it together to do that investigation by CDC and Institute of Medicine.

MS. BROWN: Your Honor, I'm not sure where this is. Can you direct me to the reliance list where it is?

MS. O'DELL: Your Honor, it specifically relates to an Institute of Medicine report that was published this year, and Dr. Clarke-Pearson saw it before, shortly after his deposition, actually. It was published recently. It was not a part of his reliance materials. But Ms. Brown, in suggesting that

talcum powder is not a risk factor recognized by the CDC, is really not accurate. The CDC commissioned a report by the Institute of Medicine. It's the National Academy of Science issued a report called "Ovarian Cancers Evolving Paradigms in Research and Care," and they concluded that talcum powder and asbestos are inflammatory risk factors of ovarian cancer. I feel like that -- putting up that website, suggesting they don't consider talcum powder, that they don't consider talcum powder as a risk factor, opened the door for us to show in fact they did.

MS. BROWN: Your Honor, I object, of course. This is the first time I'm hearing of this document. It was not included, obviously, in advance. It is not included as part of the report. It's not included as materials relied on. It's not included on a supplemental reliance list and does not form the basis of his opinion.

To the extent that counsel intended to use it, we did not have the opportunity to review it, to have our own experts comment on it. I literally have no idea what it is and it was completely not disclosed.

THE COURT: Do you have it at counsel table?

MS. BROWN: I don't.

MS. O'DELL: She does. It's PSC

Clarke-Pearson 3. We discussed it this morning. I admitted it was not on his reliance list. It was an oversight. I agreed not to use it. And then she put into play, the CDC. It would be unfair to leave the record with the suggestion that they don't consider talcum powder a risk factor when I believe that's not accurate.

THE COURT: Can I have a copy and see what that looks like?

MS. O'DELL: It's in your binder, Judge, I believe.

THE COURT: Let me take a quick look at what this is.

MS. O'DELL: Your Honor, you will see it's the National Academy of Sciences. I did bring the book, your Honor. I got copies so counsel can have one, too. If you want to see the book, I'm happy to hand that up as well.

THE COURT: This was published when? It says "Copyright 2016"?

MS. O'DELL: That's correct.

THE COURT: I want to understand what the connection between this and the CDC is.

MS. O'DELL: Let me turn to the right page.

If you'll turn to page IX in the beginning,

this Congressional mandated report sponsored by the Centers for Disease Control assesses the state of research on ovarian cancer from multiple perspectives and by multiple disciplines. So it's a CDC-sponsored document or book.

MS. BROWN: Your Honor, it is not at all a proper response to the current CDC position as available on their website right now for what are the risk factors for ovarian cancer. The proper redirect on an exhibit like this is a page from the current CDC website that says something else.

This, instead, is an older article by a different organization that was never disclosed, and no one has ever given an opinion about it, and it is also about 30 to 40 pages. So I would object as not properly in response to this at all, but, rather, an attempt to backdoor in an undisclosed exhibit that counsel gave me her word this morning it would not be used with Dr. Clarke-Pearson.

MS. O'DELL: I didn't use it on direct, your Honor. This is a page of the website. What you have in front of you is a thorough systematic review of the scientific evidence, and it's conducted in association with the National Academies of Science, an organization, I believe, if I remember correctly,

Dr. Neel said he wanted to be a part of at some point in his career.

It's authoritative. They have a section called "Inflammatory Risk Factors." It occurs on page 110, and beginning in the paragraph it says: "Studies of the inflammatory marker, c-reactive protein, suggest a possible association between inflammation and an increased risk of ovarian cancer," and I'll skip the cites for ease. "Other specific inflammatory factors have been associated with ovarian cancer. A meta-analysis reported that exposure to asbestos was associated with a 77 percent increased risk of ovarian cancer mortality," citing Camargo and the International Agency For Research on Cancer to determine that there was sufficient evidence to support a causal relationship between asbestos exposure and ovarian cancer," citing Straif. "This has led to studies of talc use which is chemically similar to asbestos and can cause an inflammatory response. The use of perineal talcum powder has been associated with 20 to 30 percent increased risk of ovarian cancer, although it has been shown to vary by histologic subtypes," citing Cramer and Terry.

MS. BROWN: You have to finish that paragraph.

MS. O'DELL: I'll be happy to.

"One analysis reported 9 percent lower ovarian cancer risk with regular aspirin use with stronger results among daily users. Trabert. However, most cohort studies have not observed a similar reduction risk. Brasky, Lacey, Murphy, Ni, Pinheiro, Prizment, and Setiawan."

That's the end of the paragraph.

MS. BROWN: Your Honor, this is not in at all -- first of all, it's just an undisclosed 30-page article that counsel and I spoke about this morning, that she said she could not find on any reliance list, and, therefore, agreed it was not appropriate to use with this witness.

And now she's attempting to get it in front of your Honor and to use it with this witness to rely on it. It's not in his report, not on materials used, not on the supplement. It has nothing to do with the CDC's web page about ovarian cancer. It's a totally different organization and it's a full report we would have to read, analyze, have our own folks take a look at. It's too late at this point, your Honor.

THE COURT: The only thing I'll do at this point is, I don't want to take testimony on the article. I'll note that the CDC current website is still not listing this on it, even though they would

have had the benefit of a report they allegedly commissioned.

So I will let you put on the record there was a report at an earlier time that did study this issue. But we also know what the CDC cites. So we'll put that out there, and we won't take questioning on it.

BY MS. O'DELL:

Q. Dr. Clarke-Pearson, since reviewing the totality of the evidence and reaching your opinions in this case, what steps have you taken to inform others about your opinion that genital use of talcum powder can cause ovarian cancer?

A. I wasn't given the opportunity to make this point --

MS. BROWN: Your Honor, there was nothing disclosed in his deposition or his report about efforts to do anything other than speak to a friend. If the testimony is going beyond that, I would object to his opinion that was not disclosed.

MS. O'DELL: It's not an opinion. It's a fact. It's what he's done. He's engaging in the medical community. There was no duty for him to stop activities following his deposition on February 4th of this year, and so I think he testified to several items that he was in the process -- several steps he

was in the process of taking, and that's what I'm asking about.

MS. BROWN: Your Honor, we had no opportunity to depose him on this. It's all brand new. At the time of his deposition, he had not done anything. If he is here today with new things he has done, it's not only beyond the scope of direct but it's an undisclosed opinion that we have not had the opportunity to depose him on and get to the bottom of and --

THE COURT: I don't think I'm getting opinions. I guess what I am going to get is, because I understand the questioning was certainly there was substantial questioning, there was nothing he had done prior to being approach by plaintiffs' counsel in this area and had not formed any opinions that there was a causal connection.

He then analyzed it, came up with his opinions, and I'm taking what you want to get now, is he being in some way proactive now to do something about his opinions? That's not more opinion. If he wants to tell me he's doing things now, I'll listen to what he's doing. I think that's where we're going.

MS. O'DELL: Yes, that's exactly it.

THE COURT: Go ahead.

THE WITNESS: So I made communication with two organizations. I have talked to Dr. Hal Lawrence, who is the CEO of ACOG, who had that one brief statement that was --

THE COURT: I don't want to hear what he may have said to you. Only what you have done.

THE WITNESS: I told him that I was serving as an expert in the plaintiffs' side, but that based on my analysis of the data that I would advise and suggest -- I can't tell ACOG what to do -- that they should investigate this in the format I would expect of the committee opinion that we were talking about earlier today. Dr. Lawrence I think --

THE COURT: I don't want to hear about that.

THE WITNESS: I also talked to Dr. Laurel Rice, who is the immediate past president of the Society of Gynecologic Oncology, and, finally, with regard to patient information, I said that the patient intake sheet in our oncology clinic doesn't include talc. We will be updating, when we finish getting rid or using up the forms we currently use in our general obstetrics and gynecology clinic at the University of North Carolina, a question about talc use, just like we have with regard to seatbelts and smoking and those risk factors.

THE COURT: That last one was an appropriate follow-up to what I asked because I asked what the forms looked like generally outside of his department.

You may proceed.

BY MS. O'DELL:

Q. Counsel put a number of magnetic labels on the board here representing organizations, and, in particular, statements they may have made to date.

To your knowledge, Dr. Clarke-Pearson, has ACOG at this point undertaken a systematic review of the scientific literature in the same way that you have to reach your opinions?

A. I do not believe they have. That's why I brought this up to Dr. Lawrence.

Q. Would it also be true that the FDA, at least at this point, has not published a systematic review of the scientific literature to date and rendered an opinion on this topic?

A. That's correct. The only thing I have seen is this letter we talked about earlier.

Q. Would it be true that the Society of Gynecologic Oncology have not undertaken a systematic review of the body of literature to reach an opinion on this subject?

A. That's true.

Q. In terms of a regulatory agency who has undertaken a systematic review, would it be fair to say that the only regulatory body that has reviewed all of the evidence and published their views of the science would be Health Canada?
A. Yes. Health Canada has done a Bradford Hill analysis.
Q. And what was their conclusion?
A. Their conclusion is very similar to my conclusion.
MS. O'DELL: That's all I have, your Honor. Thank you.
MS. BROWN: May I have a few minutes?
THE COURT: Yes.

RECROSS-EXAMINATION
BY MS. BROWN:
Q. Doctor, I want to start where counsel left off, which is the Health Canada report.
Now, at the time that you issued your opinions in this case that talc causes ovarian cancer, you had not seen the Health Canada draft risk assessment. True?
A. I don't believe I had.
Q. And you understand that the approach that Health

Canada took was a precautionary approach to decision-making that emphasizes the need to take preventive action. Right?

A. I'm not exactly sure what that means. They did an analysis, a Bradford Hill analysis based on a meta-analysis. I'm not sure what the precautionary portion that you mentioned exactly means.

Q. Do you recall answering some questions about this in your deposition?

A. I don't.

Q. Why don't we just take a look, then, at your testimony.

Do you recall agreeing that Health Canada may have made recommendations that are purely precautionary? Do you recall that?

A. I don't recall it, but if I said it in my deposition, then it would be true.

Q. Why don't we take a quick look at your deposition, page 297, lines 9 through 14.

You were asked some questions about the precautionary approach. You were asked:

"QUESTION: You understand that Health Canada may have made recommendations that are purely precautionary. Is that right?

"ANSWER: That's what I've read, yes."

Correct?
A. I guess that's what I read, but I'm not sure, as I just said, what that exactly means.
Q. Incidentally, Doctor, the Health Canada draft assessment was given to you by plaintiffs' lawyers. Correct?
A. Yes.
Q. One of the things that Health Canada in the risk assessment, the draft risk assessment, that was provided to you by counsel for the plaintiffs concluded was that
"There is a lack of an available exposure effect relationship in the human epidemiological data." Correct?
A. That's what they say.
Q. This is its most recent up-to-date analysis of the data, according to your testimony. Is that right?
A. I think, once again, looking at all the data is important.
Q. Another document that you were given by plaintiffs' lawyers, after forming your opinion that talc causes ovarian cancer, is a meta-analysis. Correct?
A. Which meta-analysis are you talking about?
Q. You were given a meta-analysis by Taher and

others by counsel for the plaintiffs after you had issued your report in this case. Is that right?
A. Yes, that's true.
Q. You did not rely on the analysis by Taher and others at the time that you issued your opinions. Correct?
A. That's correct.
Q. You understand that the Taher meta-analysis has not been peer-reviewed. Correct?
A. It has not been published. I don't know where it is in the process.
Q. Hasn't been published, not available on any journals' website. Right?
A. Not that I'm aware of.
Q. Did you undertake an analysis to figure out whether any member of the public can access this Taher meta-analysis?
A. I did not.
Q. Did you ask the plaintiffs' lawyers who gave you this meta-analysis how they got it?
A. No.
Q. Have you been to a website that the plaintiffs' lawyers maintain called "The Truth About Talc"?
A. No.
Q. Can we look at slide 36, please.

Do you know that although unpublished and un-peer-reviewed, the Taher meta-analysis is available on a website called "The Truth About Talc"? Did you know that?

A. I didn't know about the website, so I don't know anything about what was on that website.

Q. If we can go to the next slide from this website, did you know that the sponsor of the website that has access to an unpublished meta-analysis that underlies Health Canada is the Beasley Allen law firm?

A. Well, because I didn't know about the website, I didn't know anything more -- I don't know anything about the website.

Q. And in describing themselves as the sponsors of The Truth About Talc website, that has the Taher unpublished and un-peer-reviewed meta-analysis they state:

"We have the experience and resources to battle the corporate giant."

Have you seen that before?

A. I have not seen that before either.

Q. You know who Doctor Judy Wolf is. Correct?

A. I did.

Q. She is also an MDL gynecology oncologist expert like yourself. Correct?

A. That's what I understand.
Q. And in preparing for your deposition in this case, one of the things you did was review Dr. Wolf's own deposition. Right?
A. I was given that opportunity, yes.
Q. Did you also review -- if we can go to the next slide -- any of the 16 videos that Dr. Wolf has since created for The Truth About Talc web page?
A. I have not seen any of those videos and was not aware of them.
Q. So you are not then familiar with Dr. Wolf, an MDL expert's video about addressing the skeptics in the medical community?
A. I don't know what that is about, no.
Q. Did the plaintiffs' lawyers, in giving you the Health Canada assessments and the Taher assessments, did they give you a PowerPoint that was also commissioned by Health Canada?
A. No.
Q. I want to take a look at that. It's Exhibit 537. It would be in your binder, Dr. Clarke-Pearson, at 537.
Now, do you know that Dr. Krewski did --
MS. O'DELL: Your Honor, she stated this was commissioned by Health Canada. I don't know if she

intended to say that.

MS. BROWN: I'll go to the end to orient us.

Q. Do you see Dr. Krewski's name on this PowerPoint? You have never seen this PowerPoint before?

A. I have not seen the PowerPoint.

Q. Do you see that Dr. Krewski is the author of this Population Health Risk Assessment?

A. Yes.

Q. And are you aware that he is also the lead author on the Taher article that you were provided with after your deposition?

A. I was not aware of that, no.

Q. Did you -- and just to follow up on counsel's point, do you see this PowerPoint case:

"The work was conducted under a contract with Health Canada and Risk Sciences International to independently evaluate the association between talc and ovarian cancer."

Were you aware of this funding source for this PowerPoint?

A. No. I wasn't aware of the PowerPoint.

Q. I want to direct your attention to page 30 of the PowerPoint that plaintiffs' counsel produced to us a couple of weeks ago called "Cancer Classification."

Do you see that, Doctor?
A. I do.
Q. At the top is the IARC's 2010 review. Right?
A. Yes.
Q. And their conclusion that "The epidemiological studies taken together provide limited evidence of an association between perineal use of talc-based body powder and an increased risk for ovarian cancer." Correct?
A. That's what that says.
Q. Do you see the conclusion of this review which was done for a contract with Health Canada concluding that "based on this review, the criteria for classification is a Group 3 A possibly carcinogenic to humans." Do you see that?
A. Yes.
Q. And the information in the box, that "data from epidemiological studies indicate an association between exposure and human cancer but alternative explanations such as chance, bias, or confounding cannot be excluded." Do you see that?
A. Yes.
Q. Counsel for plaintiffs did not provide you with this PowerPoint that they had by the author of Taher done as a funding contract from Health Canada.

Correct?
A. Correct.
Q. And so you have not had the opportunity before coming in here to discuss Health Canada to look into what a Group 3 A possible carcinogen means under the Canadian regulatory regime. Correct?
A. I don't know anything about it.
Q. As far as you know, the Health Canada report is a draft assessment. Correct?
A. Yes.
Q. And whether or not and how, if at all, this classification plays into Health Canada's final classification is not something you know about. Correct?
A. I do not.
Q. You have not had the opportunity to look through this PowerPoint and see what the actual findings of one of the Taher's authors was, when he conducted the risk assessment. Correct?
A. Correct.
Q. That would include not having the opportunity to see what he had to say or what the group of folks conducting this risk assessment had to say about biological plausibility. Correct?
A. Is this a peer-reviewed publication?

MS. O'DELL: I object to the assertion the complete group of authors for the Taher paper contributed to this PowerPoint because that does not appear to be the case.

THE COURT: I think it says Krewski.

MS. BROWN: I'll rephrase to make sure it's the lead author of Taher.

Q. Dr. Krewski.

THE COURT: Okay.

Q. Having not been provided this PowerPoint presentation that we received a couple of weeks ago, you have not had a chance to read and interpret Dr. Krewski's thoughts or conclusions as it relates to biological plausibility. Correct?

A. I have not.

Q. Including "the specific mechanism and cascade of molecular events by which talc might cause ovarian cancer have not yet been elucidated." Correct?

A. That's what it says.

Q. You have not had a chance to look through this PowerPoint or any of Dr. Krewski's findings in this risk assessment that was done pursuant to a contract with Health Canada. Correct?

A. I have not. That's correct.

Q. You were asked some questions and you were shown

some epidemiology studies that suggested that it was possible or even plausible for particles of talc to migrate to the ovaries. Do you recall those questions?

A. Yes.

Q. And you said that in fact supported your belief that migration is possible. Correct?

A. I think it's very possible.

Q. And we spoke earlier today, though, about the conclusions from the authors of the Penninkilampi meta-analysis from 2018, the most recent one we have, that "the possible mechanism by which genital talc is associated with an increased risk of ovarian cancer hence remains unclear."

Do you remember our discussion about that?

A. I remember we discussed that. I don't remember exactly what we said.

Q. My question is: What methodology do you employ to reject the conclusions from the Penninkilampi paper that a mechanism remains unclear but to accept conclusions from other epidemiology studies that migration is the root of exposure?

A. I think I tried to explain it to the Court before. This is a discussion section in a meta-analysis. The meta-analysis was not intended to

look at biological mechanisms, potential mechanisms to determine whether there was migration or not, or whether there was anything to do with chronic inflammation or not. These are all part of a discussion after the data has been presented where the author is allowed to speculate and go on with his opinion. So this is an opinion based on their opinions. There is no reference there. But it is not part of the data that's presented in this study.

Q. So there's a bunch of references here, right?

When they are talking about the fact that NSAIDs have not consistently been associated with the decreased risk of ovarian cancer, they have a bunch of references, don't they?

A. Yes. I was talking about the last sentence you were talking about, which isn't referenced.

Q. In support of their conclusion a mechanism remains unclear, they provide a number of references; do they not?

A. They provide four references.

Q. And so what I want to understand, what methodology do you employ to reject this part of the most recent meta-analysis by Penninkilampi, that a mechanism remains unclear, but to accept similar discussions in other papers about the ability of talc

to migrate?
A. The scientific evidence and the experiments that show that other particles similar to talc can migrate to the ovaries very quickly from placement in the vagina is more scientific evidence than this opinion in the discussion section.
Q. You discussed with counsel on that score, Doctor, this Venter article. Do you remember that?
A. Yes.
Q. This is an article from 1979. Correct?
A. Right.
Q. Regarding radio tracers that were placed near a woman's cervix. Correct?
A. Yes.
Q. You know the IARC working group reviewed this article in connection with their monograph on talc?
A. I hope they did. I have to look at their reference list.
Q. And when you do, I'll represent to you you'll find that this is there, and you know that the IARC working group concluded, having, nonetheless, reviewed this 1979 study you discussed with counsel, that they concluded that the evidence of migration in a normal woman is weak. Right?
A. Yes. We went through all that, and they talked

about something about the function of the genital tract in those women undergoing surgery, which I don't understand. There is other evidence that talc is embedded in the ovary. So it gets there somehow. I think the most plausible mechanism is for it to migrate up the vagina and to the ovary and be embedded in the ovary.

Q. And the 1970 article is one on which you rely for that that opinion. Correct?

A. The radioactive article?

Q. Correct.

A. That's one of others.

Q. You spoke to counsel about some of your prior publications that do not list talc as a risk factor for ovarian cancer. Do you remember that?

A. Talking to you?

Q. I'm sorry, to counsel for plaintiffs, Ms. O'Dell -- let me reorient you.

You spoke, when Ms. O'Dell came up to ask you some more questions, she pointed out you only listed certain risk factors and not others in certain publications. Do you remember that?

A. In that review article regarding ovarian cancer screening in the New England Journal 2009.

Q. I think I heard you say that you didn't risk any

of the inflammatory risk factors. Is that right?
A. Yes.
Q. In 2011, though, remember we spoke about this, Pathways to Progress document earlier this morning?
A. Yes.
Q. You, again, had an opportunity to list them --
A. Can I explain -- I was the immediate past president of the Society of Gynecologic Oncology. I didn't write this.
Q. But before you signed your name on the cover page that was going to go on top of this report, you certainly read it. Right?
A. Yes.
Q. And this includes a discussion about risk factors that includes family history. Right?
A. Yes.
Q. And it includes one of the potentially inflammatory risk factors, obesity. Right?
A. Yes.
Q. It does not include talcum powder?
A. No.
Q. What's the relative risk for obesity and ovarian cancer?
A. I don't know that answer.
Q. Do you consider obesity to be a recognized risk

factor for ovarian cancer?
A. It's on the list of recognized risk factors, yes.
Q. You spoke to counsel about the NCI PDQ. Do you recall that?
A. Yes.
Q. I think you had some concerns that the folks doing that review were not doing a proper job doing the up-to-date evidence. Correct?
A. Yes.
Q. What is the basis for that opinion?
A. The basis of that opinion was, as we talked about a moment ago in redirect, about five papers that were cited, and I think you pointed out to me this morning or sometime today, that that PDQ is published within the last year.
Q. The PDQ itself provides a reader with some information about how frequently and the process by which the authors update this. Did you know that?
A. No, I didn't see that.
Q. Let's take a look.

On page 17 of the PDQ that we have been talking about that concludes there is inadequate evidence for perineal talc to cause ovarian cancer, we're provided with some information about how the

Board members keep up to date on the literature and update these reviews, and what we learn is that this summary is reviewed regularly and updated as necessary by the PDQ screening and prevention editorial board. Correct?

A. That's what that says. Apparently they are not keeping up, though.

Q. Board members review recently-published articles each month to determine whether an article should be discussed at a meeting, be cited with text or replaced or update an existing article that is already cited. Correct?

A. Yes.

Q. You don't have any information about the discussion or the review that went on by these board members at their monthly meetings to review the science that's contained in this PDQ?

A. I'm not privy to that conversation.

Q. (Reading.)

"Changes to the summaries are made through a consensus process in which board members evaluate the strength of the evidence in the published articles and determine how the articles should be included in the summary?"

Do you see that?

A. Yes.
Q. (Reading.)
"Any comment or questions about the summary content should be submitted to cancer.gov through the NCIs website."
Correct?
A. Yes.
Q. You told us a little bit earlier about some activities you have undertaken since your deposition. Have you emailed cancer.gov to complain about the review of the board members on this NCI review?
A. I have not because I wasn't aware of this PDQ.
Q. Doctor, when I was talking to you about this PowerPoint that you hadn't seen, I think counsel raised an objection that it only reflected the views of Dr. Krewski, the lead author, and Mr. Williams reminds me that there is in fact a page of contributors, and you see here that it includes the first named author, Dr. Taher. Correct?
A. Yes.
Q. All of the authors listed on the Taher meta-analysis. Right?
A. I believe so. I don't have the meta-analysis in front of me.
MS. BROWN: I have no further questions, your

Honor. Thank you.

FURTHER REDIRECT EXAMINATION.

BY MS. O'DELL:

Q. Dr. Clarke-Pearson, the Health Canada assessment, causal assessment, is it a comprehensive review of the scientific evidence at this time?

A. As I've read it, yes, it is. It has a Bradford Hill analysis.

Q. Does it have a Bradford Hill analysis? Is that what you said?

A. Yes.

Q. And has it been peer-reviewed?

A. I don't know one way or the other on that topic.

Q. And in that assessment, did Health Canada conclude that the connection between the genital use of talcum powder and ovarian cancer is causal?

A. Yes.

Q. And is that your opinion?

A. Yes. That supports my opinion or is my opinion.

Q. And you were shown a number of slides from a presentation by Mr. Krewski, Dr. Krewski, and this presentation --

A. This is the PowerPoint I haven't seen?

Q. Yes. The PowerPoint from a presentation that Dr. Krewski made in France.

Let me show you one of the slides you didn't have a chance to see.

This is part of Dr. Krewski's presentation, and he's walking through the Bradford Hill analysis that was undertaken.

In bullet point No. 1, included in Dr. Krewski's statistical significance presentation, it says:

"Particles of talc appear to migrate into the pelvis and ovarian tissue causing irritation and inflammation. The presence of talc in the ovaries has been documented."

A. That's what I was just saying based on the literature I have read, not this.

Q. It goes on to say:

"The specific mechanisms and cascade of molecular events by which talc might cause ovarian cancer have not yet been elucidated.

Then it goes on to say:

"Chronic inflammatory response and alteration in local immunogenicity are possible mechanisms of action of talc as a risk factor for ovarian cancer."

Is that consistent with your opinion?

A. Yes.

Q. Ms. Brown showed you a picture of a website, The

Truth About Talc. You haven't seen that website before?

A. No.

Q. Did anything that Ms. Brown presented to you during her opportunity to do recross, did that change your opinions in this case?

A. No, it does not.

MS. O'DELL: Thank you very much, your Honor.

THE COURT: Thank you. You may step down. We're done.

(Witness excused.)

(Court adjourned at 4:30 p.m.)

///

I N D E X

C E R T I F I C A T E

PURSUANT TO TITLE 28, U.S.C., SECTION 753, THE FOLLOWING TRANSCRIPT IS CERTIFIED TO BE AN ACCURATE TRANSCRIPTION OF MY STENOGRAPHIC NOTES IN THE ABOVE-ENTITLED MATTER.

S/Vincent Russoniello
Vincent Russoniello, CCR
Certificate No. 675

Q